Dissertation on

"ASSESSMENT OF THYROID FUNCTION IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS AND ITS CLINICAL CORRELATION "

Submitted in partial fulfillment for the Degree of

M.D.GENERAL MEDICINE

BRANCH - I

INSTITUE OF INTERNAL MEDICINE

MADRAS MEDICAL COLLEGE

THE TAMIL NADU DR.MGR MEDICAL UNIVERSITY

CHENNAI - 600003

APRIL 2016

CERTIFICATE

This is to certify that the dissertation entitled **"ASSESSMENT OF THYROID FUNCTION IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS AND ITS CLINICAL CORRELATION"** is a bonafide original work done by **Dr.VELVIZHI.M,** in partial fulfillment of the requirements for M.D.GENERAL MEDICINE BRANCH -I examination of the Tamilnadu Dr.M.G.R Medical University to be held in April 2016 , under my guidance and supervision in 2015

Prof.Dr.K.SRINIVASAGALU M.D.,
Director
Guide and Professor
Institute of Internal Medicine
Madras Medical College & RGGGH
Chennai - 600003

Prof.Dr.R.VIMALA M.D.,
Dean
Madras Medical College &
Rajiv Gandhi Government Hospital,
Chennai - 600003

DECLARATION

I hereby solemnly declare that the dissertation entitled **"ASSESSMENT OF THYROID FUNCTION IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS AND ITS CLINICAL CORRELATION"** is done by me at Institute of Internal Medicine, Madras Medical College & Rajiv Gandhi Government General Hospital , Chennai during 2015 under the guidance and supervision of **Prof.Dr.K.SRINIVASAGALU, M.D.,** This dissertation is submitted to The Tamilnadu Dr. M.G.R Medical University , Chennai towards the partial fulfillment of requirement for the award of M.D.Degree in General Medicine (Branch I)

Place :

Date :

Dr.VELVIZHI. M
Post graduate student ,
M.D. General Medicine,
Institute of Internal Medicine,
Madras Medical College &
RGGGH, Chennai - 600003

ACKNOWLEDGEMENT

I express my heartful gratitude to the Dean, **Prof. Dr. R. VIMALA M.D.**, Madras Medical College & Rajiv Gandhi Government General Hospital, Chennai-3 for permitting me to do this study.

I am very grateful to **Prof. Dr. K. SRINIVASAGALU M.D.,** Director and Professor of Medicine, Institute of Internal Medicine, Madras Medical College & Rajiv Gandhi Government General Hospital, Chennai-3 who guided and trimmed my work throughout the period of my study.

I am deeply indebted to **Prof. Dr. K. RAJESWARI M.D DM**., Professor and Head of Department , Department of Rheumatology, Madras Medical College & Rajiv Gandhi Government General Hospital, Chennai-3 for her support and guidance.

I am very much thankful for the help rendered by my Assistant Professors **Dr.D.K.SIVAKUMAR, M.D.,** and **Dr.P. BALAMANIKANDAN M.D.,** for their constant help and encouragement.

I am extremely thankful to all the Members of the **INSTITUTIONAL ETHICS COMMITTEE** for giving approval for my study.

I express my heartful gratitude to **Dr.N.SUJATHA, Dr.BHARATH RAJ KIDAMBI** and **Dr.MANOJKUMAR** for their constant support and encouragement.

I also thank all the patients who were part of the study and my Professional colleagues for their support and criticisms

CONTENTS

INTRODUCTION

INTRODUCTION

SLE is a chronic inflammatory disease of unknown aetiology which involving multiple organs of the body .It mainly affects the women of child bearing age group and the ratio of 10 to 15:1 (female : male), mainly due to estrogen which modulates the lymphocyte activation[1] .

The genetic susceptibility with environmental factor promotes immune system activation and damages the organ that contributes to the clinical manifestation, morbidity and occasionally mortality[2,3].

There is an accelerated progression of atherosclerosis in patients with SLE due to chronic inflammation which promotes inflammatory mediators and cytokine release which leads to vascular and endothelial dysfunction causes decreased compliance of the blood vessels and promotes atheromatous plaque formation, The presence of thyroid dysfunction among SLE patients further aggrevates this condition.[45]

.

AIMS AND OBJECTIVES

AIM AND OBJECTIVES

- To study the prevalence of thyroid dysfunction in patients with SLE.
- To measure Free T3, Free T4, TSH in serum.
- To emphasize the role of routine thyroid function testing in patients with SLE.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

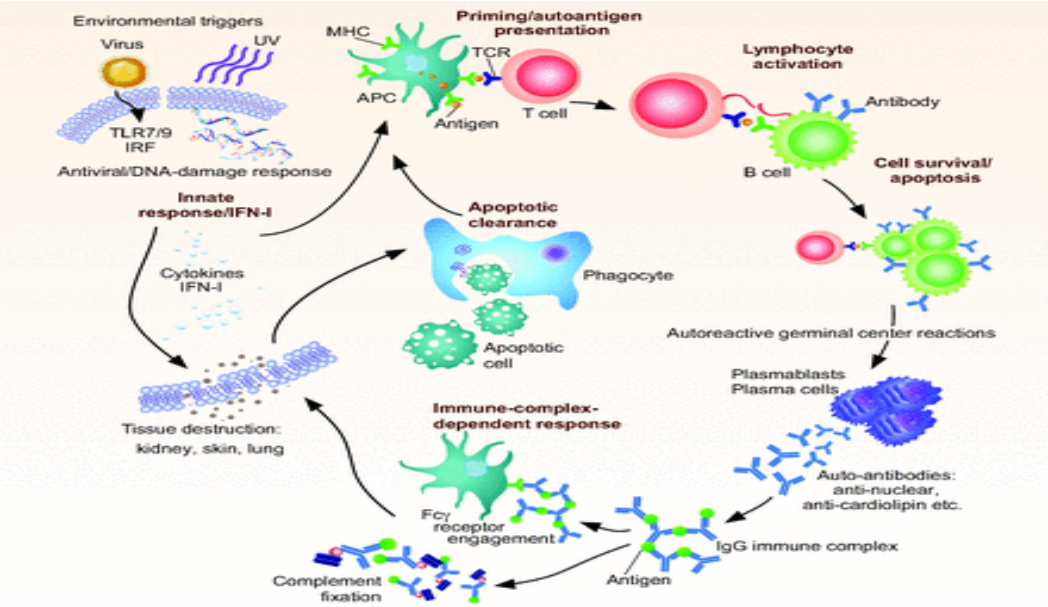
PREVALENCE:

The prevalence of disease is more common in Asian , African-American and Hispanic population which is three to four fold higher when compared to white populations .It is rare in African blacks . Its prevalence rate ranges from 20 - 240 per 1,00,000 persons .

HISTORICAL ASPECTS :

The word "Lupus"as derived from Latin word - ‘wolf’ which is coined by a physician Rogerius who describes the erosive lesion of face which is a reminiscent of wolf's bite and "Erythematosus" from Greek word means red color.[4-7] The skin lesions are described by Thomas, Bateman, Cazenave and Moriz Kaposi in nineteenth century. Kaposi proposed the two types of lupus erythematosus as discoid form and a disseminated form. The disseminated or systemic form of lupus was firmly established by the work of Osler in Baltimore and Jadassohn in Vienna in 1904 .[8]

PATHOGENESIS :

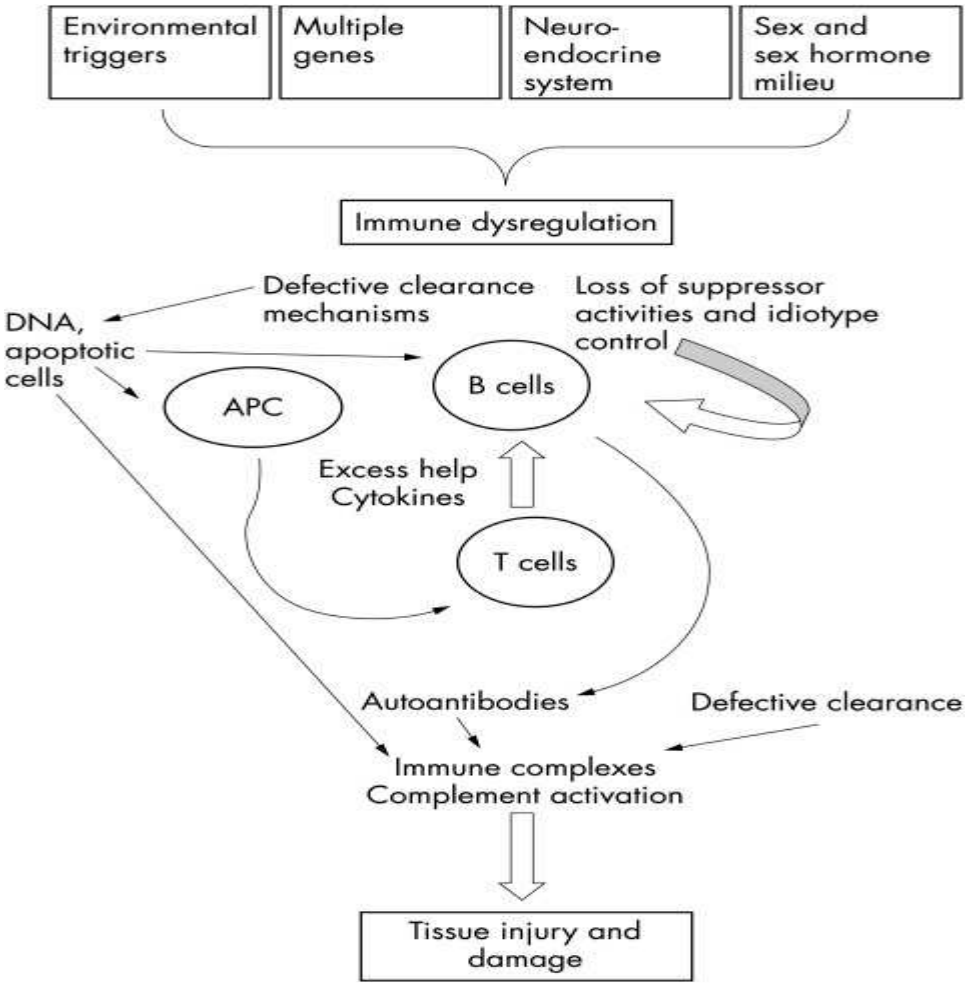


The susceptible genes and environmental factors leads to abnormal immune system activation which includes,

1) Abnormal activation pathways and decreased activation thresholds in adaptive immunity cells such as mature B lymphocytes and Tlymphocytes.
2) Impaired clearence of apoptotic cells and immune complexes.
3) Innate immune system activation y protein self antigen , viral RNA / DNA
4) Defective regulation of B cells, CD4, CD8 and myeloid suppressor cells.

Due to this immune dysregulation there is increased production of Interleukin 17 and 10, Interferon 1 and 2, tumor necrosis factor α (TNFα), B cell maturation and cytokines B lymphocytes.

There is decreased production of Interleukin 2 and Transforming growth factor β (TGF β), all these factors contribute to autoantibody production and complement activation leads to release of inflammatory cytokines, oxidants and vasoactive products which leads to target tissue damage in multiple organs .[9-12]



AETIOLOGY :

Definite :

Ultraviolet B light [13]

Probabale :

Prolactin and Estrogen[1]

Drugs :[13]

1) Methyldopa
2) Isoniazide
3) Minocycline
4) ACE inhibitor
5) Beta blocker
6) Hydantoins
7) Hydralazine
8) Procainamide
9) Propafenone
10) Chlorpromazin
11) Penicillamine
12) Disopyramide
13) Interferon-α
14) Tumor necrosis factor inhibitors

POSSIBLE : [14-17]

1) Smoking
2) Vitamin D deficiency
3) Infectious agents other than Epstein Bar Virus
4) HIV
5) Bacterial DNA
6) Bacterial lipopolysaccharides
7) Endotoxins
8) Silica [18]
9) Pristane and other hydrocarbons

DIETARY FACTORS :

Alfalfa sprouts and canavanine containing foods.

GENETIC FACTORS :

Genetic Variants Associated with Significant Risk for Systemic Lupus Erythematosus		
Gene	Genomic Location	Proposed Function
HLA	6p21.33 and 6p21.32	Presentation of antigen
ITGAM	16p11.2	Adhesion of monocytes and polymorphonuclear cells to endothelial cells
IFR5	7q32.1	Production of interferon-α
KIAA1542	11p15.5	Linkage disequilibrium with IRF7; production of type I interferon
PXK	3p14.3	Unknown protein kinase effect
PTPN22	1p13	Inhibition of leukocyte activity
FCGR2A	1q23	Clearance of immune complexes
STAT4	2q32	Modulation of the production of cytokines in T-cells and natural killer cells; activation of response of macrophages to interferon-α
BLK	8p23.1	Activation of B cells

HLA = *Histocompatibility antigen;* ITGAM = *Integrin-α_m (also known as CD11b, Mac-1 and complement receptor 3);* IFR5 = *interferon regulatory factor 5;* KIAA1542, PXK *were not defined further in any source;* FCGR2A = *Fc receptor for IgG;* PTPN22 = *protein tyrosine phosphatase receptor type 22;* STAT4 = *signal transducer and activator of transcription 4; and* BLK = *B-cell specific tyrosine kinase.*

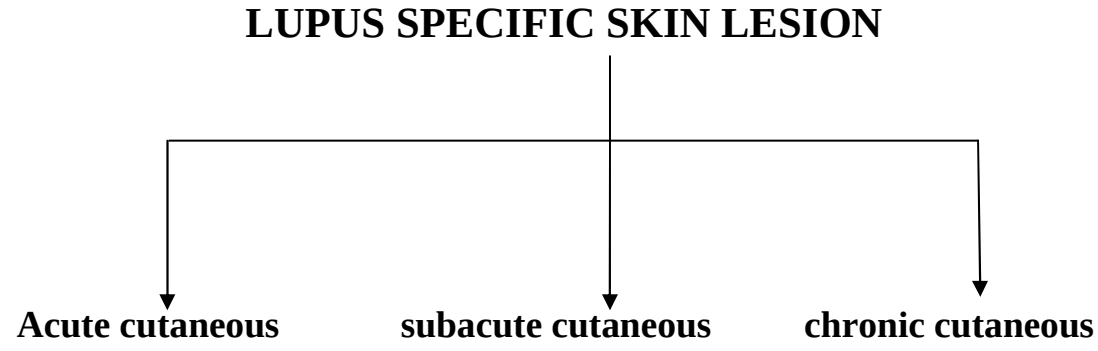
Table adapted from Crow MK, New England Journal of Medicine.

SYSTEMIC MANIFESTATIONS OF SLE :

Systemic lupus erythematosus is an autoimmune disease with varying presentations from mild disease to life threatening disease characterised by relapsing and remitting course with multisystem involvement having variable prognosis. The comorbidities of SLE is described based on the system affected.

MUCOCUTANEOUS MANIFESTATIONS :

It is the most common manifestation which occurs in 80 - 90% patients of SLE. Photosensitivity and oral ulcers are common in SLE patients. It is classified into lupus specific and lupus non specific skin lesions .[19,20]



ACUTE CUTANEOUS ERYTHEMATOSUS :

The butter fly rash is a hallmark of acute skin lesion and is confined to the malar area sparing nasolabial fold. The most commonly involved site is palmar, dorsal and extensor aspect of the hands. It classically involves the space between interphalangeal joints and spares the metacarpophalangeal joints where it heals without scarring.[19,20]

SUBACUTE ERYTHEMATOSUS :

It presents either as annular lesion with central clearing and peripheral scaling or papulosquamous lesion .It mainly affects shoulder, back, neck and extensors of the arm where it spares the face. The lesion lasts for weeks to months and is also non scarring .The antibody associated with annular type is anti-SSA/Ro, [21] where paraneoplastic syndrome is also associated with subacute erythematous lesion.[22]

CHRONIC CUTANEOUS ERYTHEMATOSUS :

The commonest type of chronic cutaneous lupus is discoid lupus erythematosus (DLE) which is further classified into generalised discoid involves above and below the neck, the other type is localised predominantly affects head and neck. The lesion appears as disc shape so it is named as discoid. The characteristic finding is follicular plugging. Lupus profundus, lupus panniculitis and chilblain lupus are other chronic cutaneous lupus lesions. It histologically resembles as squamous cell carcinoma .[23]

NON SPECIFIC LUPUS SKIN LESIONS :

- Vasculitis
- leg ulcer
- cutis laxa
- urticaria
- Rheumatoid nodule
- Sclerodactyl
- Non scaring alopecia
- Acanthosis nigricans
- Erythema multiforme
- Lichen planus
- Non scaring bullous eruptions24

NON SCARRING BULLOUS LESION which is a rare manifestation of systemic lupus erythematosus.

MUSCULOSKELETAL :

Arthralgia and polyarthritis are the commonest manifestations. Joint deformities and erosions are rare in SLE[25] . Myalgia is very common but myositis is rare .[26]

Avasular necrosis of bone can also occur in SLE .[27]

RENAL :

It is the most common cause for morbidity and mortality in SLE .[28] The clinical presentation varies from asymptomatic proteinuria or hematuria to frank nephrotic syndrome or glomerulonephritis which is rapidly progressing with significant loss of renal function The lupus nephritis usually occurs within first three years of the disease .The pathological evidence occurs in 90% cases of SLE whereas the clinical nephritis develops only in 50% cases .It is necessary to screen for nephritis in patients with active SLE at regular three months interval period. The lupus nephritis is classified by International Society Of Nephrology.[29] Renal biopsy is mandatory for SLE patients with nephritis .Most of the patients with lupus nephritis will prone for accelerated atherosclerosis over a period of years of the disease so it is necessary to control inflammation , hyperlipidemia and blood pressure.

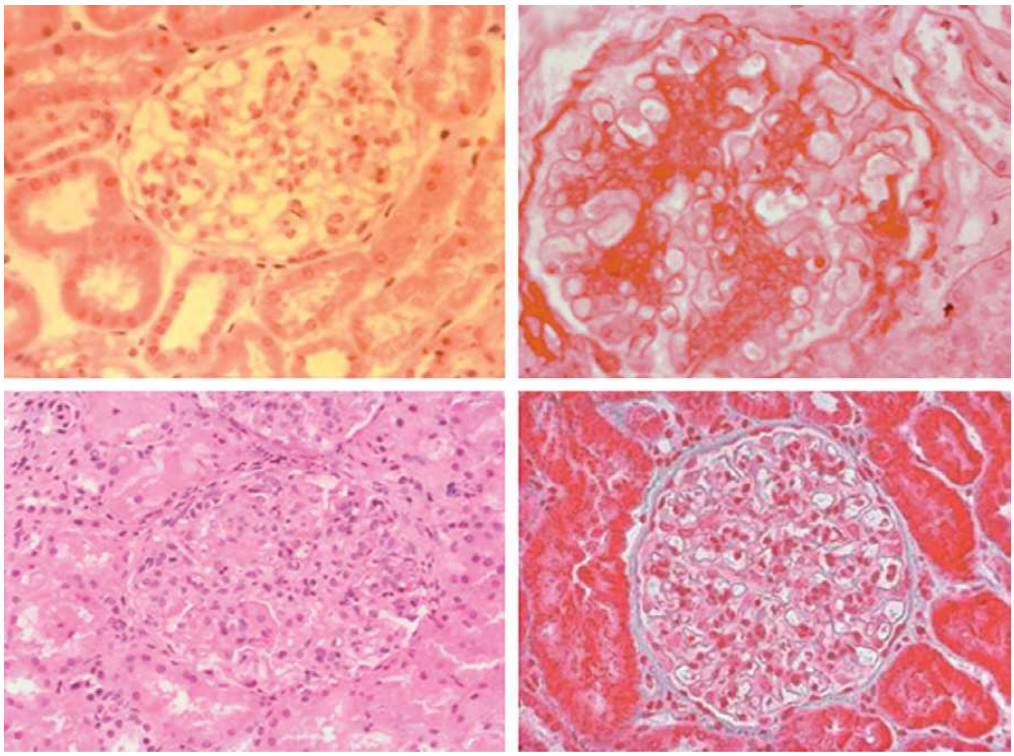
LUPUS NEPHRITIS CLASSIFICATION :

(INTERNATIONAL SOCIETY OF NEPHROLOGY AND RENAL PATHOLOGY SOCIETY) [29]

Table 1. Classification of Glomerulonephritis in Systemic Lupus Erythematosus

Class	Definition
I	• *Minimal mesangial LN* • *Normal glomeruli by LM, but mesangial immune deposits by IF*
II	• *Mesangial proliferative LN* • Mesangial hypercellularity with mesangial immune deposits.
III	• Focal LN • III (A): Purely active lesions: focal proliferative LN • III (A/C): Active and chronic lesions: focal proliferative and sclerosing LN • *III (C): Chronic inactive with glomerular scars: focal sclerosing LN*
IV	• Diffuse LN • IV-S (A) or IV-G (A): Purely active lesions: diffuse segmental (S) or global (G) proliferative LN • IV-S (A/C) or IV-G (A/C): Active and chronic lesions: diffuse segmental or global proliferative and sclerosing LN • *IV-S (C) or IV-G (C): inactive with glomerular scars: diffuse segmental or global sclerosing LN*
V	• *Membranous LN*
VI	• Advanced sclerosing LN • ≥ *90% of glomeruli globally sclerosed without residual activity*

A **B**



C **D**

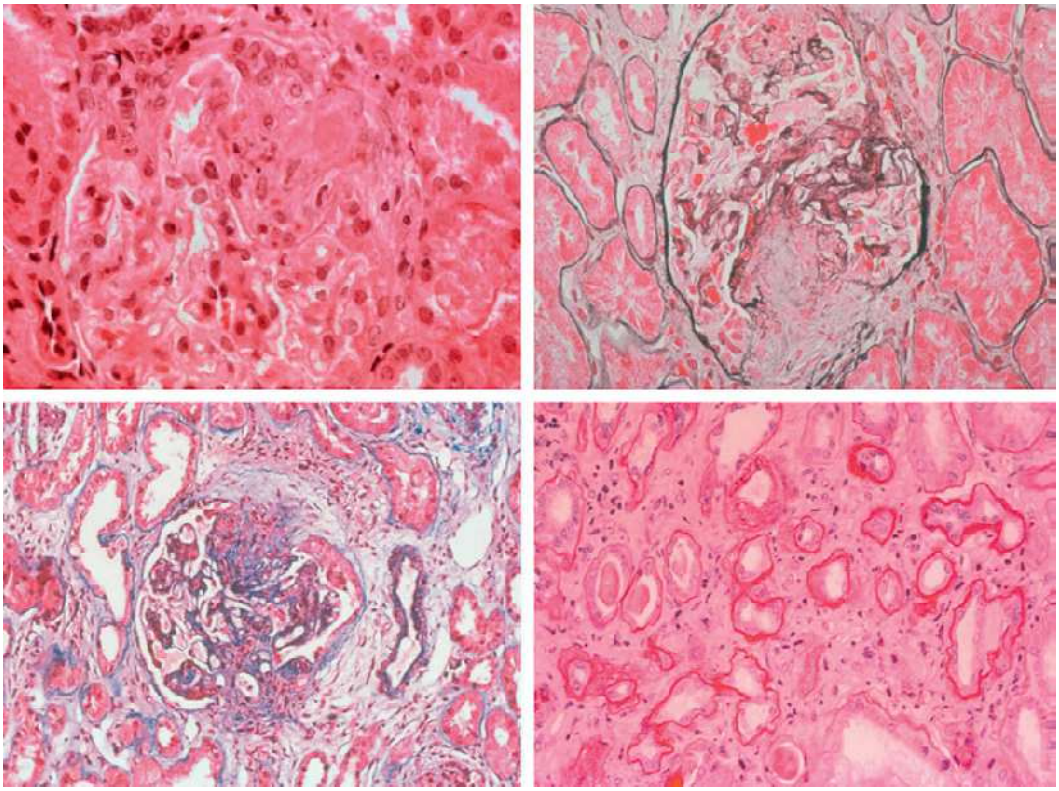
A) Normal glomerulus

B) Mesangial proliferative (Type II)

C) Proliferative Nephritis which shows mesangial and endocapillary hypercellularity with lobular appearance of glomerular tufts and patent capillary loops , (Type III -Focal , Type IV - Diffuse)

D) Membranous nephropathy (Type V) - the capillary walls are prominent and widely patent resembles "stiff structure with decreased compliance.

E **F**



G **H**

E) Fibrinoid necrosis with karyorrhexis in focal proliferative glomerulonephritis.

F,**G)** Cellular crescents with endothelial proliferation and monocytes lining Bowman's capsule with a predominantly mononuclear interstitial infiltrate.

H) Severe interstitial fibrosis and tubular atrophy. Tubular basement membrane thickening and epithelial degeneration with deposition of collagenous connective tissue .

PULMONARY MANIFESTATIONS:

Pleuritis is the commonest manifestation which occurs in 50% cases of SLE and correlates with active disease. [30] Other manifestations are pleural effusion pneumonitis, diffuse alveolar haemorrhage , chronic interstitial lung disease, [31] shrinking lung syndrome [32] and pulmonary arterial hypertension .

CARDIOVASCULAR SYSTEM :

It usually involves pericardium , coronary arteries , valves and myocardium. Pericarditis manifests in more than 50% of patients. [33] Valvular insufficiency and Libman-Sacks endocarditis can also occur in SLE patients .The risk of coronary artery disease is higher in patients with SLE due to chronic inflammation and oxidative damage to the arteries which accelerates atherosclerosis .

VASCULAR :

The risk of vascular events are three to tenfold higher in SLE patients especially in women less than 49 years of age. Myocardial infarction, vasculitis, transient ischaemic attacks and stroke cases have been described in SLE patients .[37]

GASTROINTESTINAL SYSTEM :

Nausea, vomiting , diarrhoea and elevated liver enzymes can occur in active disease of SLE . Auoimmune peritonitis , pancreatitis and Intestinal vasculitis is more prevalent in SLE patients which produces life threatening events like ischaemia, perforations , bleeding and sepsis. [34,35]

HEMATOLOGY :

Anaemia is more common in patients with SLE . It usually affects all three cell lineages. Autoimmunehemolytic anaemia, Idiopathic thrombocytopenic purpura, Lymphadenopathy and spleenomegaly are also more common among SLE patients.[36]

OCCULAR :

Keratoconjunctivitis sicca is the most frequent occular complication of SLE.[37] Other serious manifestations includes optic neuritis and retinal vasculitis which leads to blindness.

CENTRAL NERVOUS SYSTEM : [38]

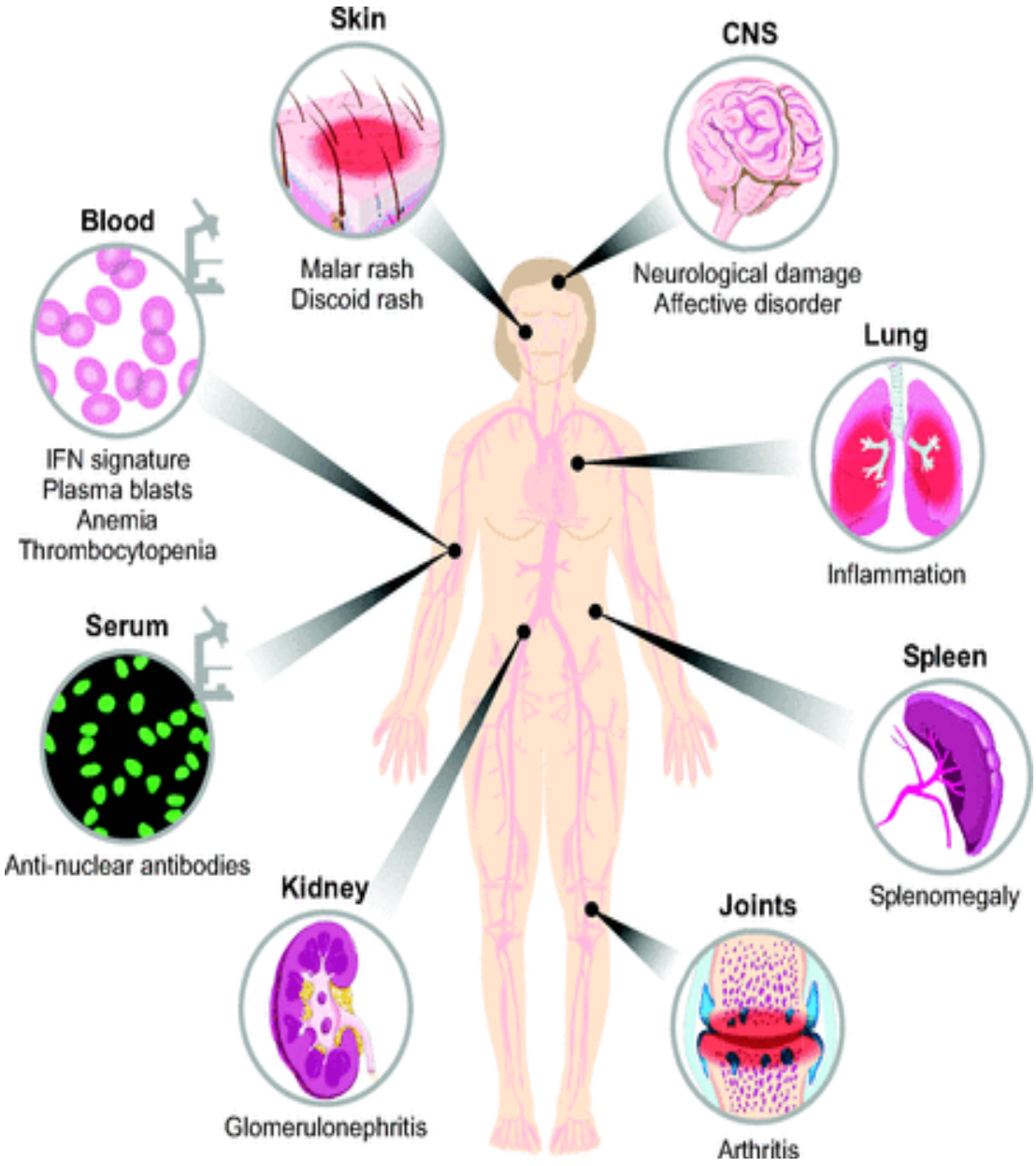
Classification of Neuropsychiatric Syndromes in Systemic Lupus Erythematosus

Central Nervous System	Peripheral Nervous System
Aseptic meningitis	Guillain-Barré syndrome
Cerebrovascular disease	Autonomic disorder
Demyelinating syndrome	Mononeuropathy, single/multiplex
Headache	Myasthenia gravis
Movement disorder	Cranial neuropathy
Myelopathy	Plexopathy
Seizure	Polyneuropathy
Acute confusional state	
Anxiety disorder	
Cognitive dysfunction	
Mood disorder	
Psychosis	

THYROID AND SLE :

Thyroid dysfunction is more prevalent in patients with SLE when compared to the general population and is mainly due to the production of antibodies such as antithyroglobulin and antimicrosomal antibodies. SLE patients are more prone for developing hypothyroidsm rather than hyperthyroidsm .

CLINICAL MANIFESTATION :



DIAGNOSTIC CRITERIA OF SLE :

1997 ACR criteria	
Malar rash	Fixed erythema, flat or raised, over the malar eminences
Discoid rash	Erythematous circular raised patches with adherent keratotic scaling and follicular plugging; atrophic scarring may occur
Photosensitivity	Exposure to ultraviolet light causes rash
Oral ulcers	Includes oral and nasopharyngeal ulcers, observed by physician
Arthritis	Nonerosive arthritis of two or more peripheral joints, with tenderness, swelling, or effusion
Serositis	Pleuritis or pericarditis documented by ECG or rub or evidence of effusion
Renal disorder	Proteinuria >0.5 g/d or 3+, or cellular casts
Neurologic disorder	Seizures or psychosis without other causes
Hematologic disorder	Hemolytic anemia or leukopenia (<4000/L) or lymphopenia (<1500/L) or thrombocytopenia(<100,000/L) in the absence of offending drugs
Immunologic disorder	Anti-dsDNA, anti-Sm, and/or anti-phospholipid
Antinuclear antibodies	An abnormal titer of ANA by immunofluorescence or an equivalent assay at any point in time in the absence of drugs known to induce ANAs

If 4 of these criteria, well documented, are present at any time in a patient's history, the diagnosis is likely to be SLE

ANTIBODIES IN SLE :

Table 1—*Autoantibodies Commonly Present in Sera of Patients With Systemic Lupus Erythematosus**

Autoantibody	Frequency of Occurrence	IIF Pattern in Hep-2 Cells	Clinical Associations
SLE-specific			
dsDNA	30-90% SLE	Nucleoplasmic, homogeneous	Virtually diagnostic of SLE; lupus nephritis, in some patients parallels disease activity
Sm	15-30% SLE	Nucleoplasmic, coarse-speckled	Associated with U1-RNP antibodies; virtually exclusively present in SLE
SLE-nonspecific			
Histones	50-70% SLE; >95% drug-induced SLE	Nucleoplasmic, homogeneous	Associated with anti-DNA antibodies
Ro/SSA	24-60% SLE	Nucleoplasmic, fine-speckled	Subacute cutaneous SLE, neonatal lupus syndrome, SLE with C2 and C4 deficiencies; 18% PM-DM, 5% SSc, 5% RA
LA/SSB	9-34% SLE	Nucleoplasmic, fine-speckled	Present in 90% mothers with infants born with neonatal lupus syndrome
U1RNP	30-40% SLE; almost all patients with MCTD	Nucleoplasmic, coarse-speckled	Often present in association with anti-Sm antibodies; presents features of SLE, scleroderma, and/or DM/PM

*MCTD = mixed connective tissue disease; RA = rheumatoid arthritis.

TREATMENT :

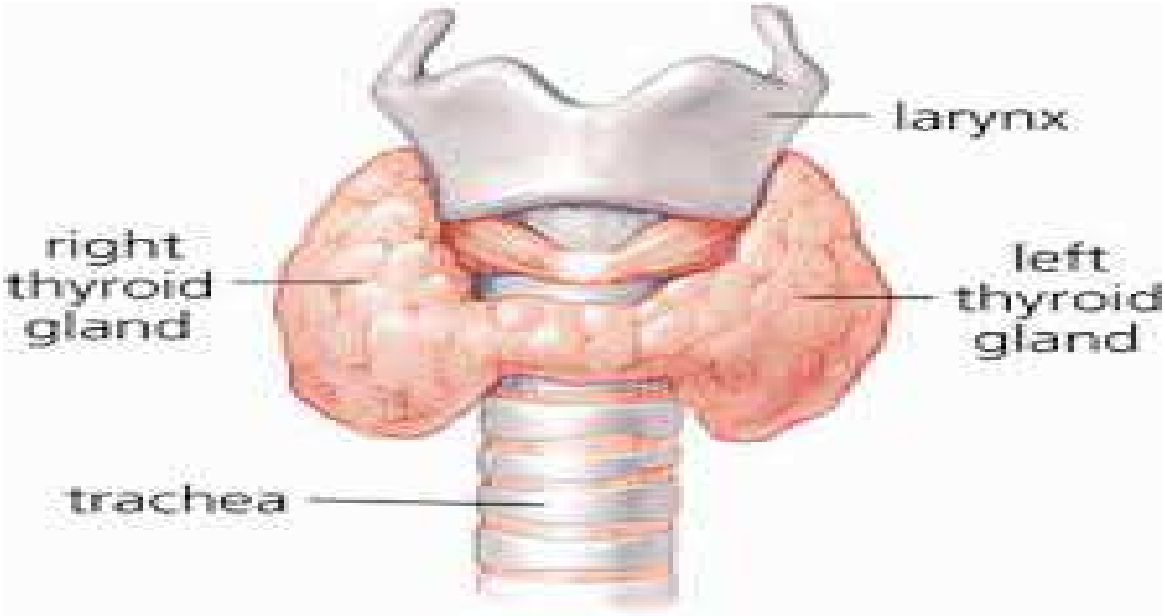
Disease Severity	Induction Therapy	Maintenance Therapy
Mild	High-dose GC (0.5-1 mg/kg/day prednisone ×4-6 wk, tapered to 0.125 mg/kg every other day within 3 mo) alone or in combination with AZA (1-2 mg/kg/day)	Low-dose GC (prednisone ≤0.125 mg/kg on alternative days) alone or with AZA (1-2 mg/kg/day)
	If no remission within 3 mo, treat as moderately severe	Consider further gradual tapering at the end of each year of remission
Moderate	MMF (2 g/day) (or AZA) with GC as above; if no remission after the first 6-12 mo, treat as severe	MMF tapered to 1.5 g/day for 6-12 mo and then to 1 g/day; consider further tapering at the end of each year in remission
		Alternative: AZA (1-2 mg/kg/day)
Severe	Pulse IV-CYC alone or in combination with pulse IV-MP for the first 6 mo (background GC 0.5 mg/kg/day for 4 wk, then taper)	Quarterly pulses of IV-CYC for at least 1 year beyond remission
	If no response, consider adding RTX or switch to MMF	Alternative: AZA (1-2 mg/kg/day), MMF (1-2 g/day)

AZA, azathioprine; CYC, cyclophosphamide; GC, glucocorticoid; IV, intravenous; MMF, mycophenolate mofetil; MP, methylprednisolone; RTX, rituximab.

THYROID :

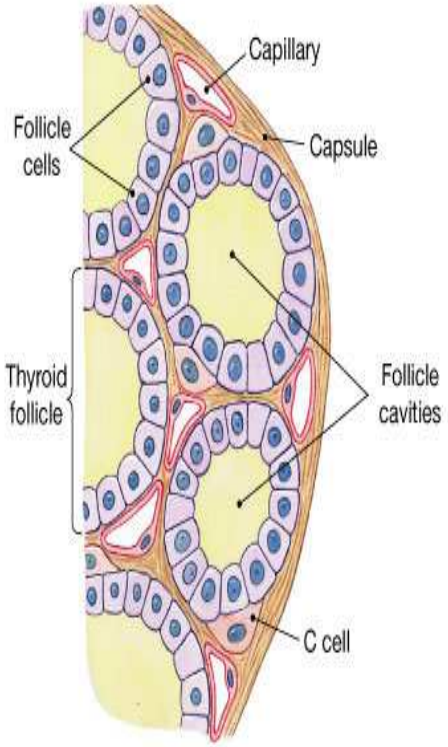
ANATOMY AND DEVELOPMENT

The name of thyroid was described from Greek word (thyreos-shield, eidos-form). It is the first endocrine gland to develop which occurs in the third week of gestation. It arises from floor of primitive pharynx. The gland is butterfly shape and is situated in the anterior part of the neck extends from C5-T1 between the suprasternal notch and cricoid cartilage. The weight of the gland is 12-20 grams and is brownish red in colour with rich blood supply. It is composed of two lobes joined by isthmus. The thyroid medullary C cells arises from ultimobronchial body of neural crest .[39]

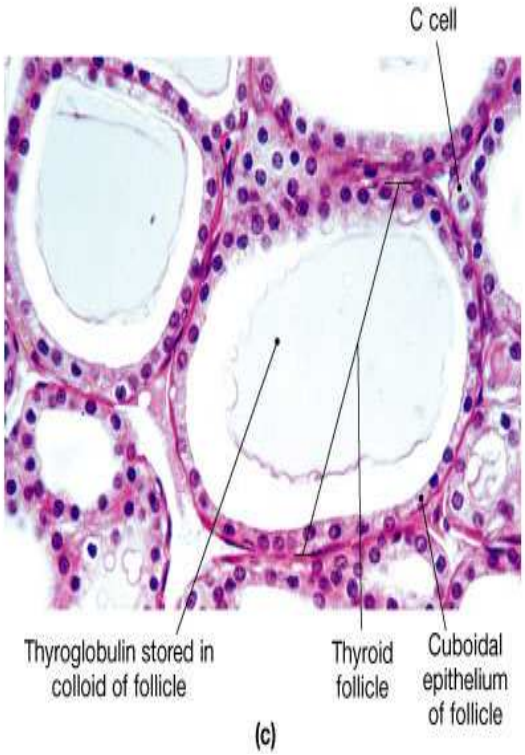


HISTOLOGY :

Gland is composed of hollow spheres, called colloid follicles. Squamous epithelial cells, cuboidal cells (follicle cells) Colloid fills the follicle cavities Follicle cells produce thyroglobulin ----→ TH



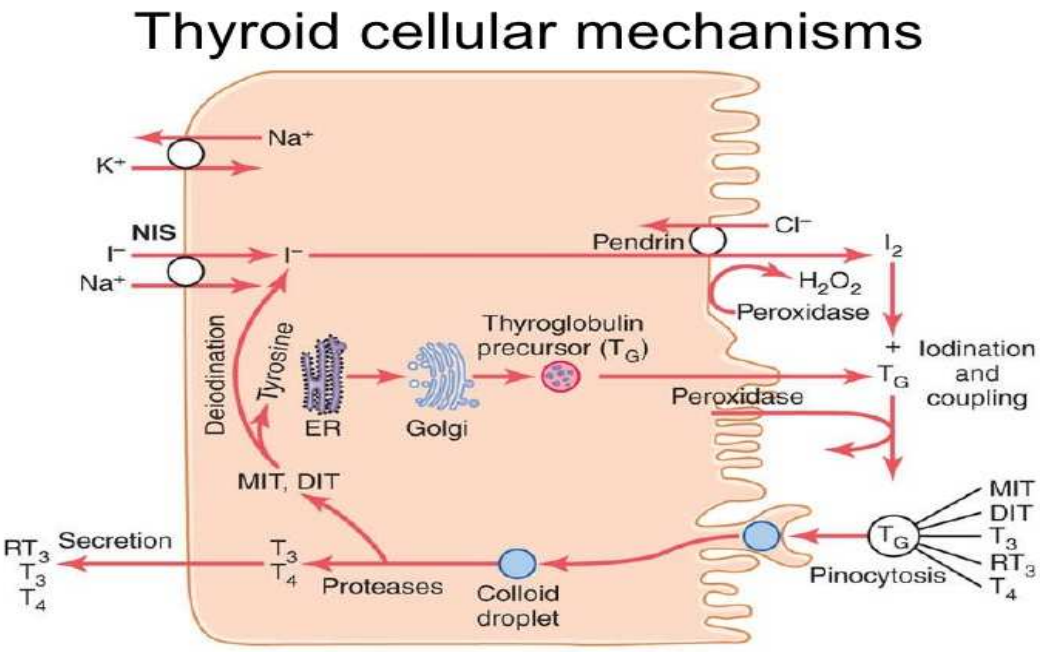
(b)



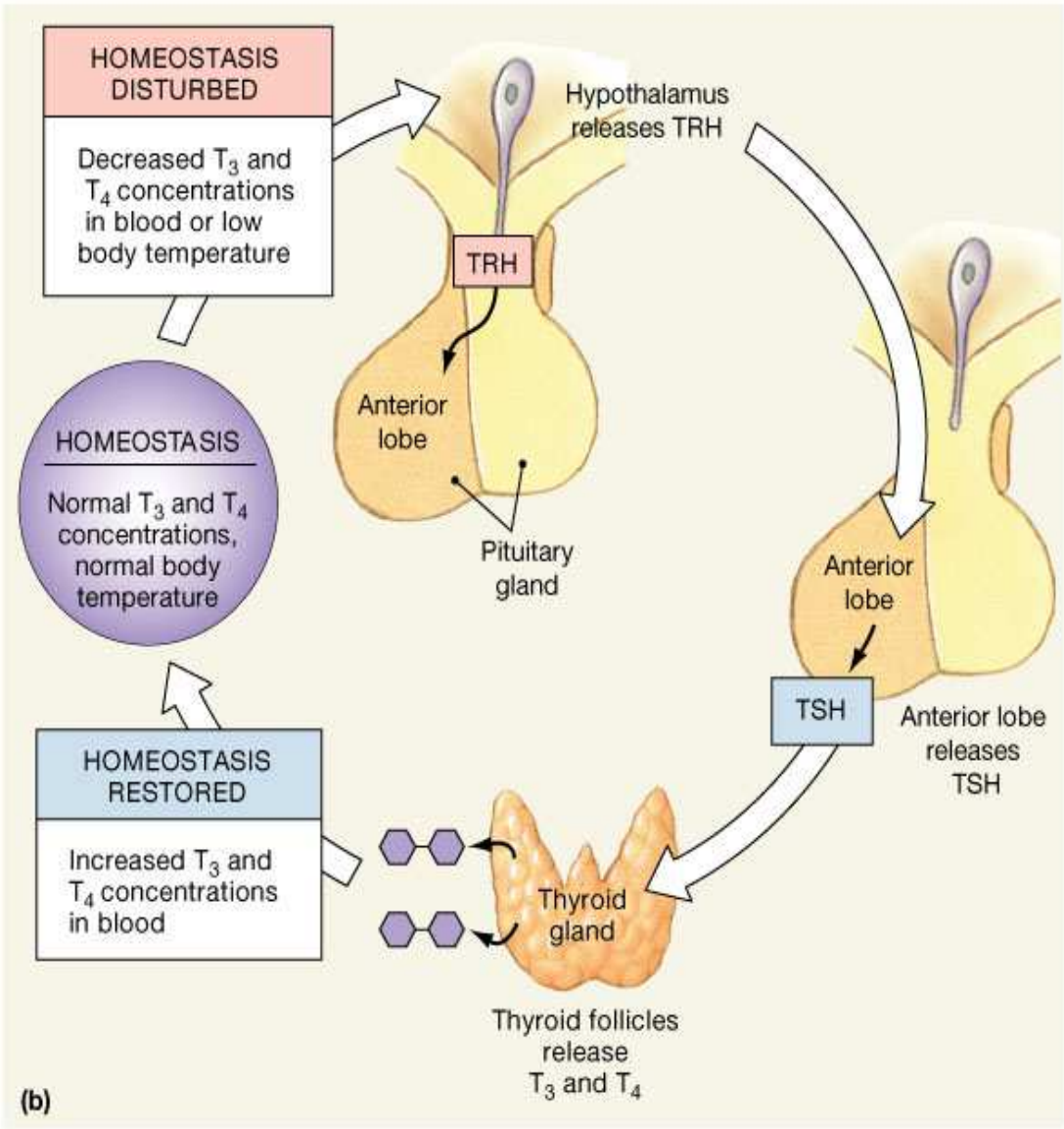
(c)

PHYSIOLOGY :

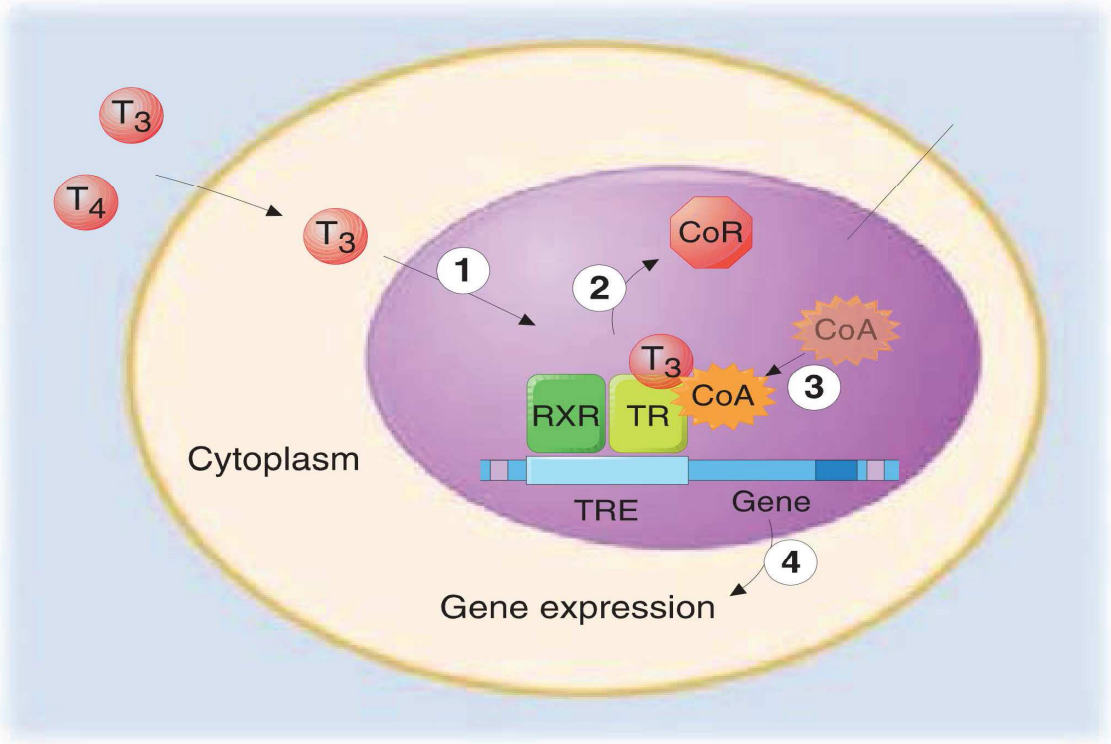
The synthesis of thyroid hormone usually starts during 11th week of gestation. It secretes two principle hormones, namely triiodothyronine (T3) and thyroxine (T4) where T3 is also secreted from the peripheral tissue by deiodination of T4. The thyroid gland contains follicular cells which secretes thyroglobulin, a precursor of thyroid hormones. The secretion of T4 is twenty times higher than T3 which is more active than T4 .[40]



THYROID AXIS : [41]



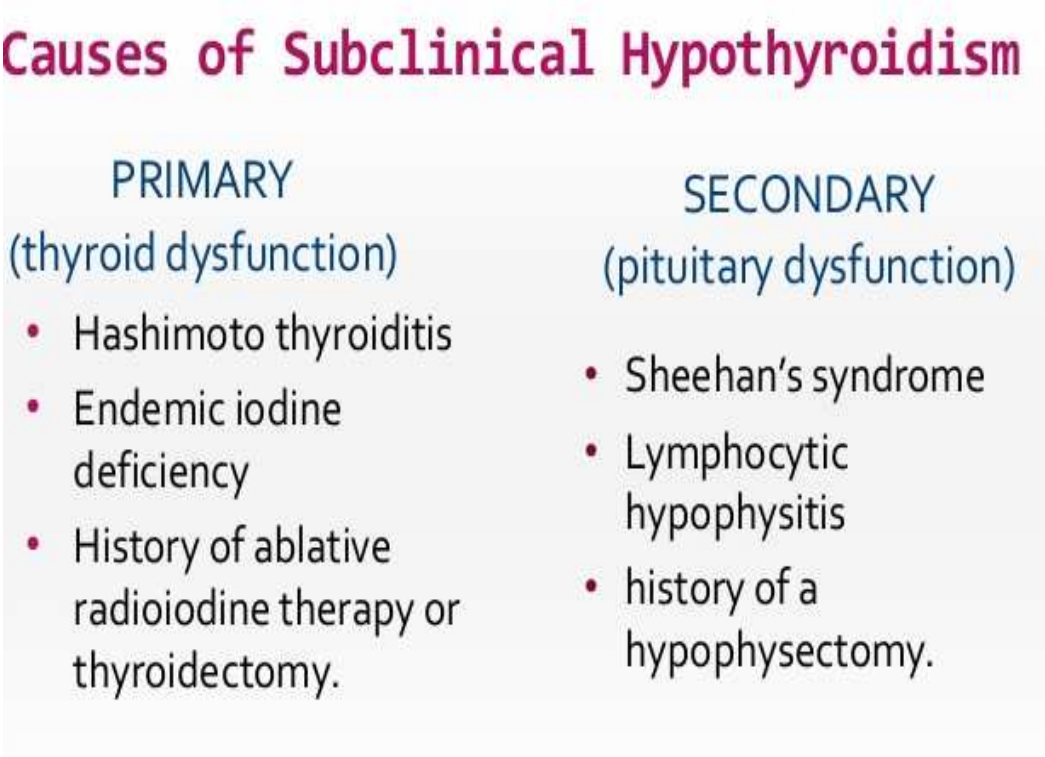
HORMONE ACTION :

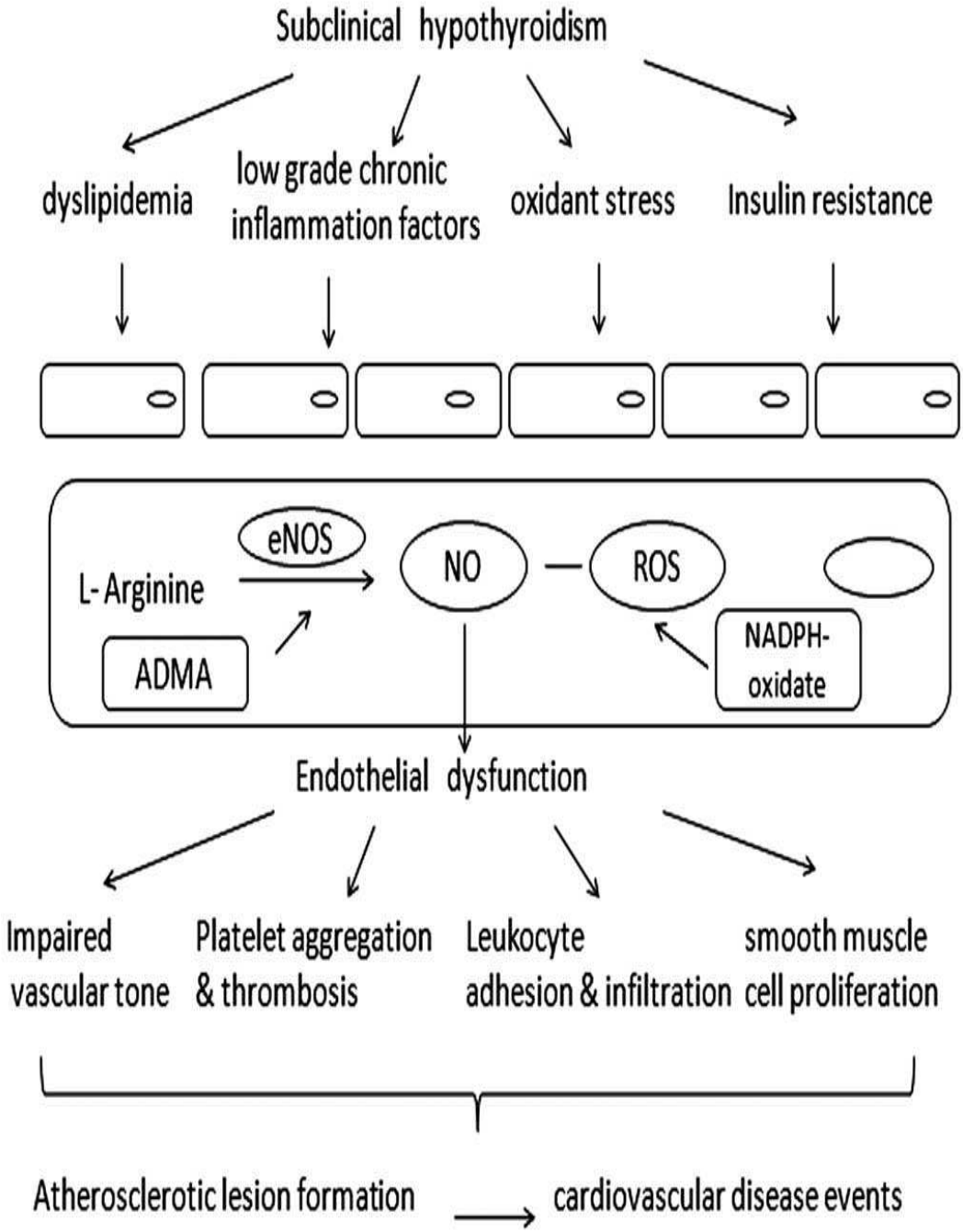


Thyroid hormone enters into the nucleus of the cells which binds to DNA sequence termed as thyroid response elements (TRE) of thyroid hormone receptors (TR), especially T3 has higher affinity for binding with receptor than T4. The hormone receptor complex either increases or decreases the gene expression which codes for enzyme that regulates cell function.[42]

SUBCLINICAL HYPOTHYROIDISM :

The patients are clinically asymptomatic with elevated TSH level usually less than 10 mU/L and low normal free T4 level .




Subclinical hypothyroidism
dyslipidemia
low grade chronic inflammation factors
oxidant stress
Insulin resistance
eNOS
L- Arginine
ADMA
NO
ROS
NADPH-oxidate
Endothelial dysfunction
Impaired vascular tone
Platelet aggregation & thrombosis
Leukocyte adhesion & infiltration
smooth muscle cell proliferation
Atherosclerotic lesion formation
cardiovascular disease events

CAUSES OF HYPOTHYROIDISM :

PRIMARY HYPOTHYROIDISM:

Acquired :

Autoimmune : Hashimotos thyroiditis (SLE ,RA)

Postablative thyroiditis

Infitrative thyroid disorders : Amyloidosis , scleroderma ,

Hemochromatosis , sarcoidosis , cystinosis ,

Riedels struma,

Endemic goitre

Congenital :

TSH receptor mutation

Agenesis or Dysplasia of thyroid

Organification disorders

NIS or Pendrin mutations

Idiopathic TSH unresponsiveness

SECONDARY HYPOTHYROIDISM:

- Hypothalamic disorders : trauma, tumors, infiltrative disease, idiopathic
- Pituitary disorders : Sheehans syndrome, infitrative disorders, trauma, post surgery or irradiation , pituitay hormonal deficiency . Bexarotene treatment

TRANSIENT HYPOTHYROIDISM :

Subacute thyroiditis

Silent thyroiditis like postpartum thyroiditis

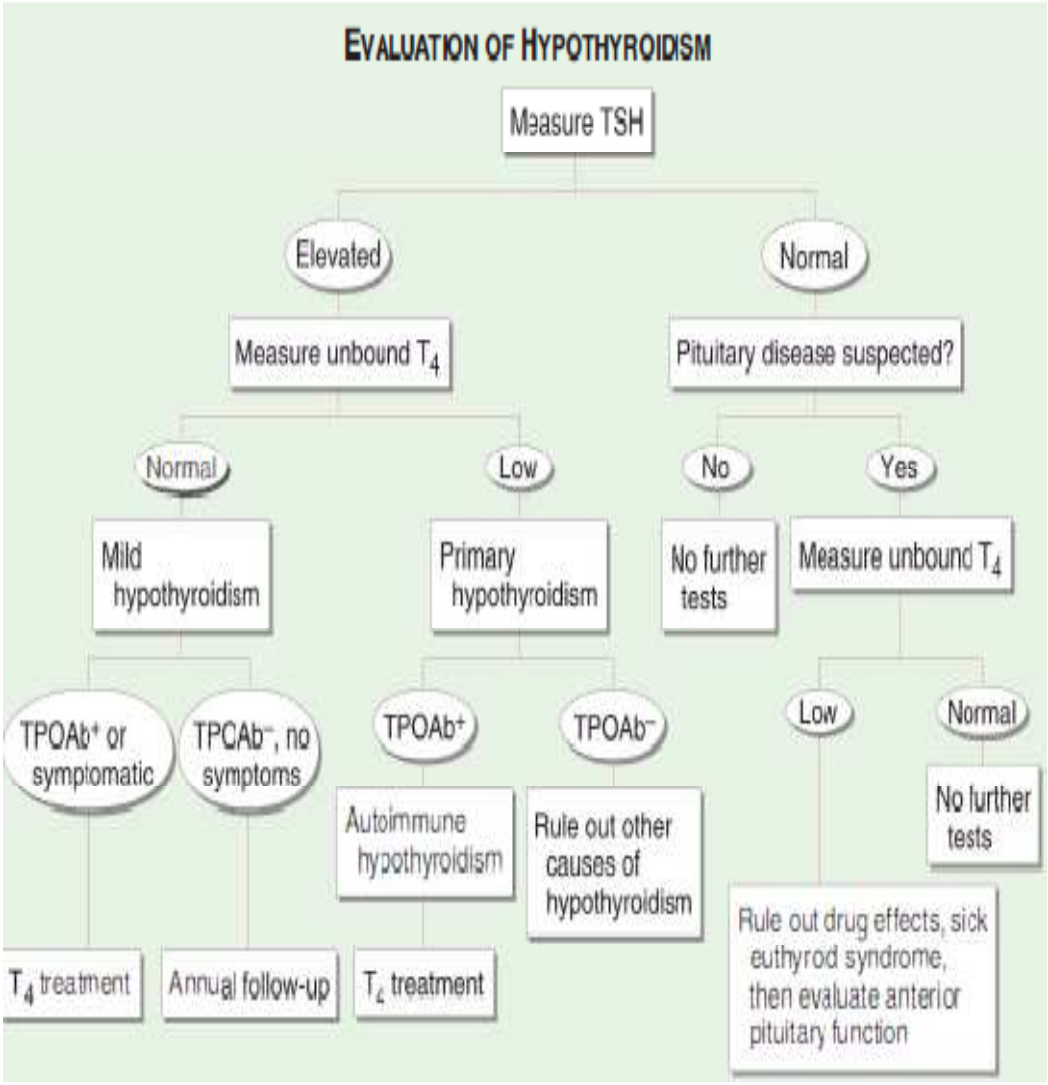
After subtotal thyroidectomy or ^{131} I treatment in Graves disease .

SYMPTOMS OF HYPOTHYROIDISM :

1. Hair loss
2. Hoarseness of voice
3. Dry skin
4. Impaired hearing
5. Dyspnea
6. Cold intolerance
7. Weight gain
8. Decreased appetite
9. Poor memory
10. Tiredness , weakness
11. Menorrhagia
12. Paraesthesia
13. Hearing impairment
14. Constipation

SIGNS OF HYPOTHYROIDISM :

1) Diffuse alopecia
2) Dry coarse skin
3) Peripheral edema
4) Myxedema
5) Carpal tunnel sydrome
6) Bradycardia
7) Delayed tendon reflexes
8) Polyserositis



TPO^- - Thyroid peroxidase antibody present

TPO^+ - Thyroid peroxidase antibody absent

TSH - Thyroid stimulating hormone

TREATMENT OF HYPOTHYROIDISM: [43]

Subclinical hypothyroidism :

- If the TSH is persistently elevated for more than 3 months start treatment with levothyroxine 25-50 microgram.
- In pregnancy treatment has to be initiated immediately.

Overt Hypothyroidism :

- Levothyroxine 1.6microgram per kg usually 100 -150µg, should be taken 30 minutes before breakfast.
- Goal of the treatment is to normalise the TSH.

Myxedema coma :[44]

Levothyroxine IV - 500microgram as a loading dose, then followed by 50-100microgram/day plus parenteral hydrocortisone of 50mg every 6th hourly.

Treat hypothermia and electrolyte disturbances like hyponatremia or hypoglycemia.

CAUSES OF HYPERTHYROIDISM :

PRIMARY HYPERTHYROIDISM :

1) Graves disease

2) Toxic adenoma

3) Toxic multinodular goitre

4) Jod-Basedow effect (iodide induced)

5) Drug induced - Lithium , Amiodarone

6) Struma ovarii

7) Iatrogenic over replacement

8) TSH receptor mutation

9) McCune - Albright syndrome (mutation of Gsα)

SECONDARY HYPERTHYROIDISM :

1) Pituitary tumors - TSH secreting tumors

2) Pregnancy

3) Chorionic gonadotropin secreting tumors

THYROTOXICOSIS WITHOUT HYPERTHYROIDISM :

1) Silent thyroiditis

2) Subacute thyroiditis

3) Thyrotoxicosis factitia

4) Radiation

SUBCLINICAL HYPERTHYROIDISM :

It is referred as, clinically asymptomatic patient with normal free thyroid hormones and subnormalTSH level which is <0.1 mU/L .It can progress to hyperthyroidism if not recognized ealier and treated promptly. The prevalence is about 0.7% of the population.

SYMPTOMS OF HYPERTHYRODISM :[45]

1) Fatigue and weakness

2) Excessive sweating

3) Heat intolerance

4) Weight loss

5) Increased appetite

6) Palpitations

7) Irritability

8) Hyperactivity

9) Dysphoria

10) Polyuria

11) Diarrhoea

12) Loss of libido

13) Oligomenorrhea

SIGNS :

1) Tremor

2) Warm and moist skin

3)Tachycardia

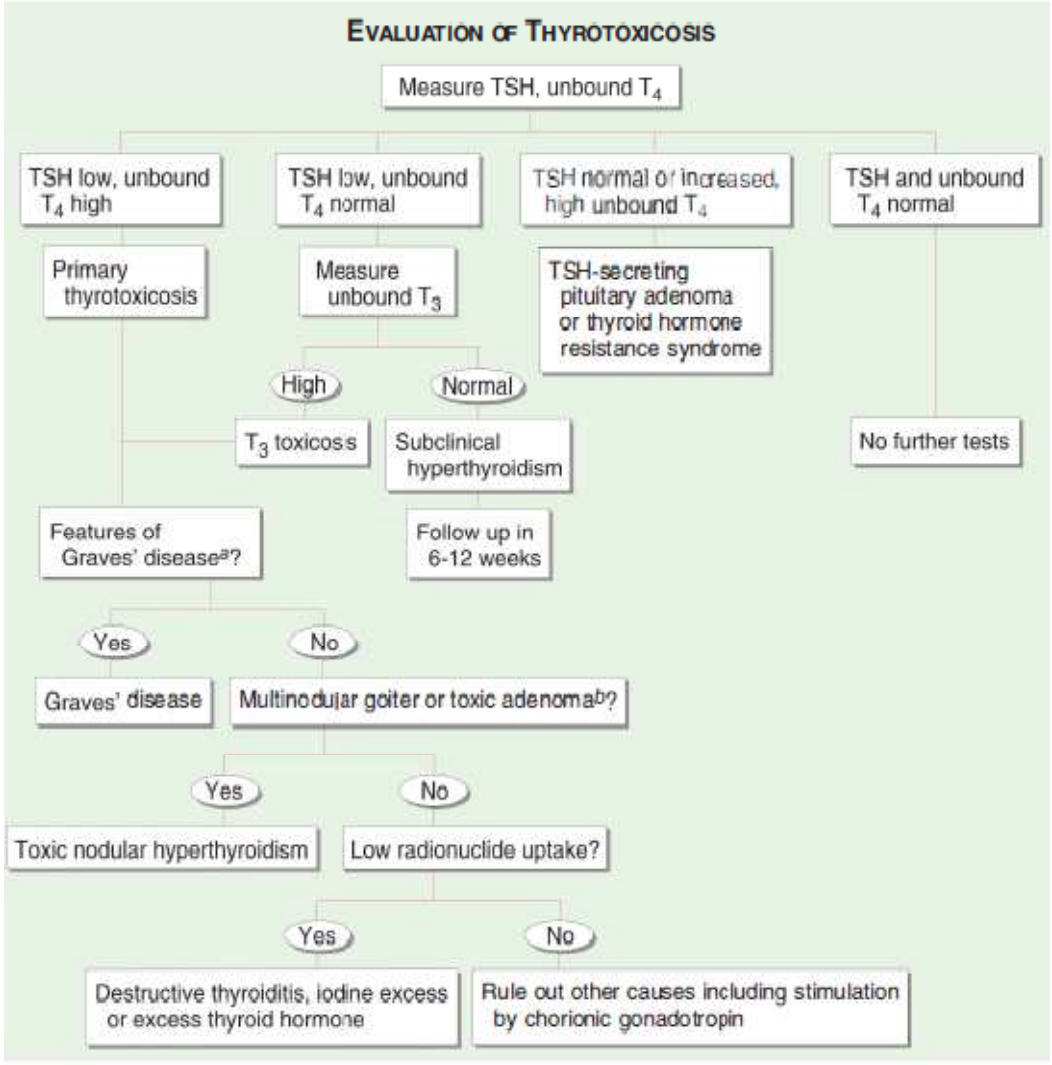
4) Atrial fibrillation

5) Gynecomastia

6) Goitre

7) Lid retraction or lag

8) Proximal myopathy


EVALUATION OF THYROTOXICOSIS
Measure TSH, unbound T_4
TSH low, unbound T_4 high
TSH low, unbound T_4 normal
TSH normal or increased, high unbound T_4
TSH and unbound T_4 normal
Primary thyrotoxicosis
Measure unbound T_3
TSH-secreting pituitary adenoma or thyroid hormone resistance syndrome
High
Normal
T_3 toxicosis
Subclinical hyperthyroidism
No further tests
Features of Graves' disease[a]?
Follow up in 6-12 weeks
Yes
No
Graves' disease
Multinodular goiter or toxic adenoma[b]?
Yes
No
Toxic nodular hyperthyroidism
Low radionuclide uptake?
Yes
No
Destructive thyroiditis, iodine excess or excess thyroid hormone
Rule out other causes including stimulation by chorionic gonadotropin

MATERIALS & METHODS

MATERIALS AND METHODS

SOURCE OF DATA :

Patients admitted in Department of Rheumatology , Madras Medical college and Rajiv Gandhi Government General Hospital , Chennai -3 diagnosed to have systemic lupus erythematosus , fulfilling the inclusion and exclusion criteria were included in the study group .100 such patients were taken up for this study .

STUDY DESIGN :

A hospital based observational study

STUDY DURATION :

6 months

INCLUSION CRITERIA :

Proven cases of Systemic lupus erythematosus by clinical and biochemical evidence .

EXCLUSION CRITERIA :

Patients with known case of hypothyroidism , hyperthyroidism SLE patients with thyroid disorder on treatment.

DATA COLLECTION AND METHODS :

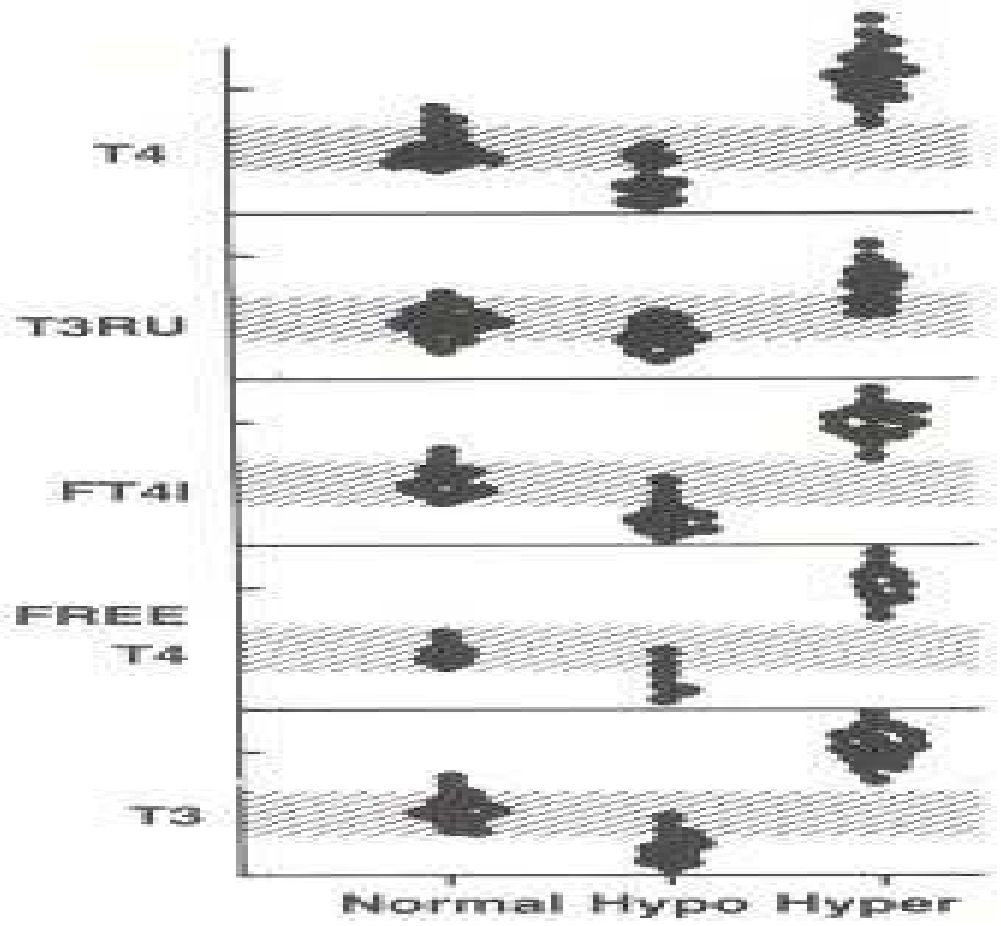
Data was collected in a pretested proforma from eligible patients. 100 patients were selected on the basis of simple random sampling. They were subjected to detailed history taking and clinical examination. The following investigations were done.

- Haemogram
- ESR
- LFT
- RFT with electrolytes
- Urine Routine
- Lipid profile
- Electrocardiogram
- Chest X -ray
- ANA
- Anti ds-DNA
- Free T3
- Free T 4
- TSH
- USG Neck

THYROID FUNCTION TEST :

Thyroid function test was done by a single vein puncture and the blood sample is collected for assessing thyroid function by measuring FT3,FT4 and TSH level using radioimmunoassay method .The most accurate test to diagnose hypothyroidism and hyperthyroidism is serum TSH level where it is the first hormone to be affected in thyroid gland failure.I t usually depends upon the thyroid hormone level in the serum , so it is better to assess the TSH level along with T4 orT3 .FT4 is the physiological active form where it enters into the tissue and acts within it. The last hormone to be affected in thyroid disorder is T3 .

- TSH level is elevated in hypothyroidism and decreased in hyperthyroidism.
- FT3 and FT4 level decreased in hypothyroidism and increased in hyperthyroidism .
- Normal FT4 -0.7-1.7ng/d
- Normal FT3 -0.2-0.5ng/dl
- Normal TSH -0.4-4.2mU/L



STASTICAL METHODS APPLIED :

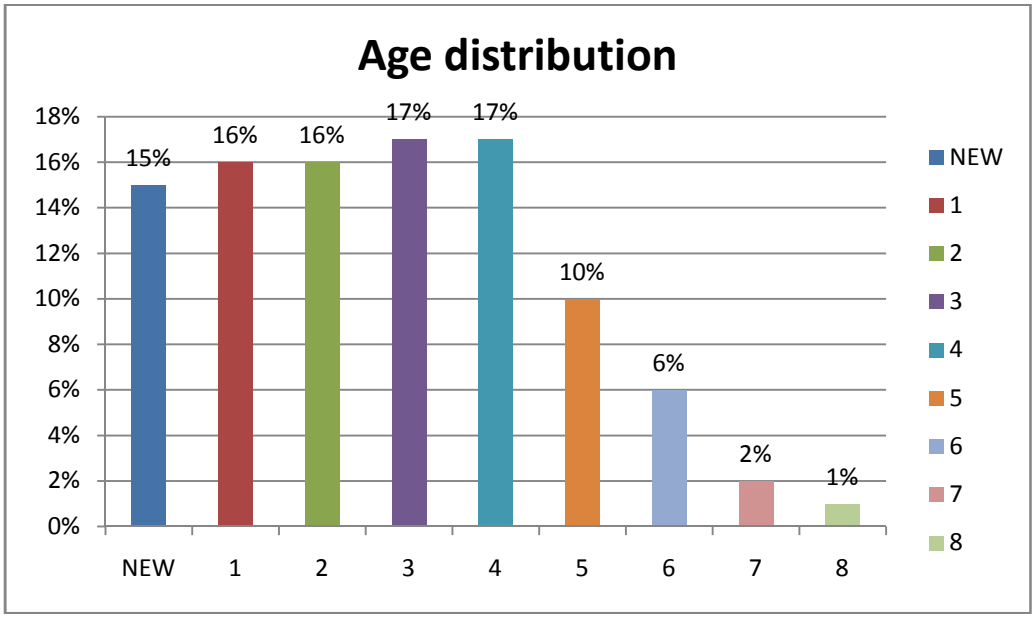
Datas were analysed using the SPSS software. Stastical significance was indicated by the Chisquare test. Variables were considered to be significant if $p<0.05$.

OBSERVATION AND RESULTS

OBSERVATION

AGE DISTRIBUTION

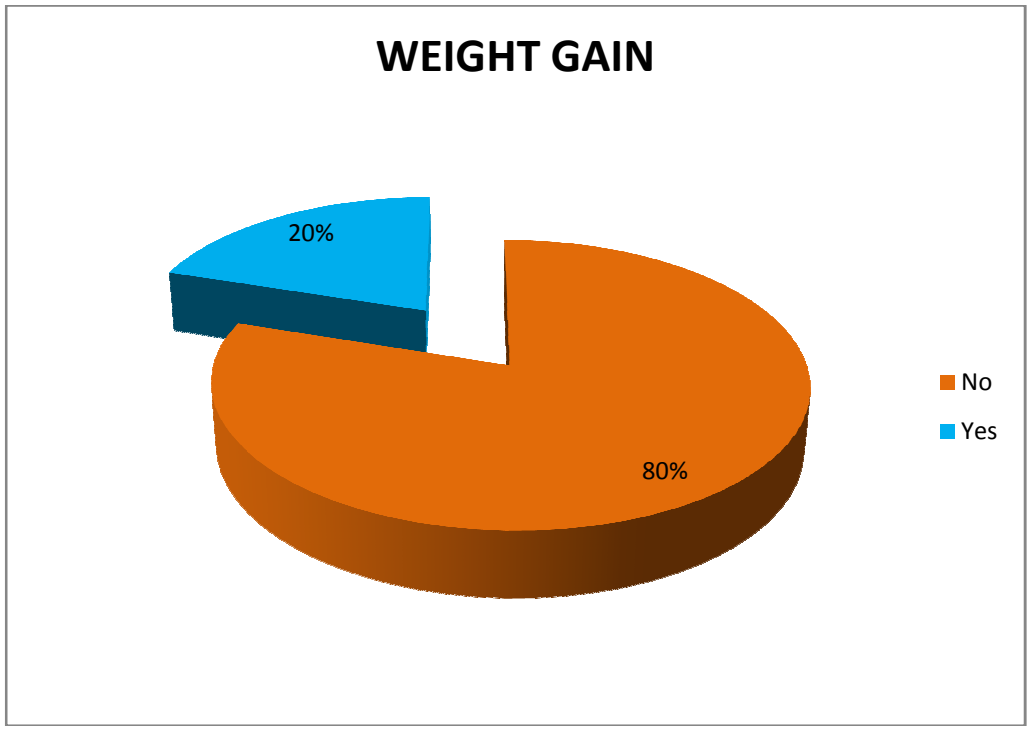
AGE	Frequency	Percent
15-20	18	18.0
20-30	45	45.0
30-40	31	31.0
40-50	6	6.0
Total	100	100.0



Most cases of SLE (45 Patients) occur in the age group of 20-30 (45%) years.

WEIGHT GAIN

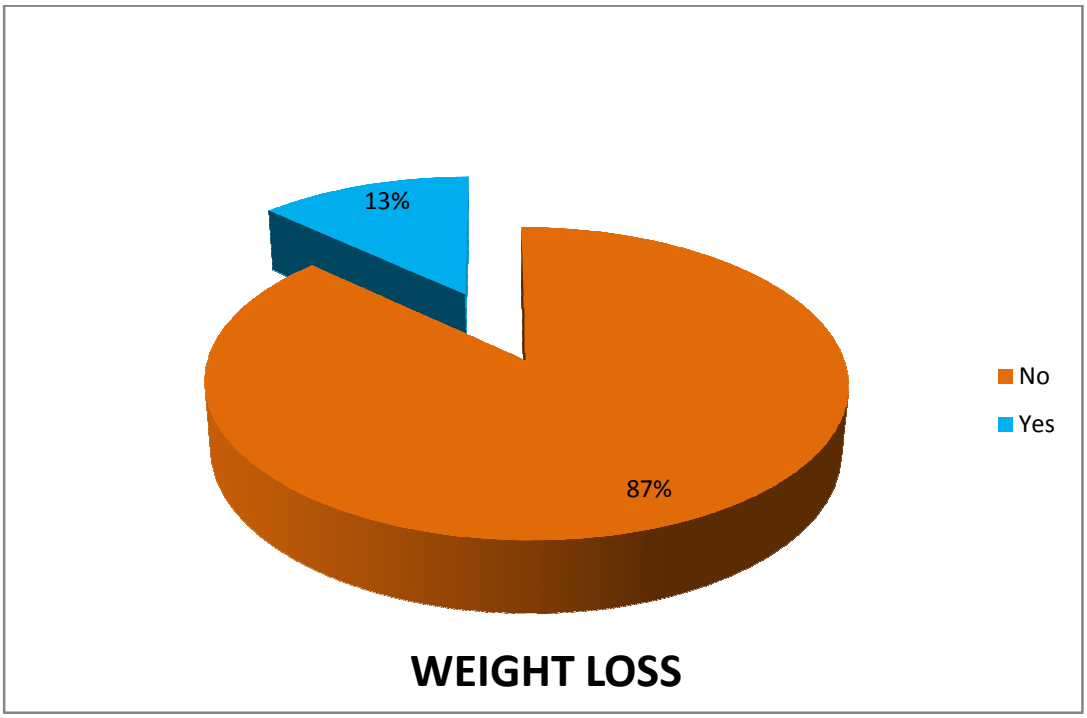
		Frequency	Percent
Valid	No	80	80.0
	Yes	20	20.0
	Total	100	100.0



Among 100 patients included in our study, 20 (20%) patients had weight gain.

WEIGHT LOSS

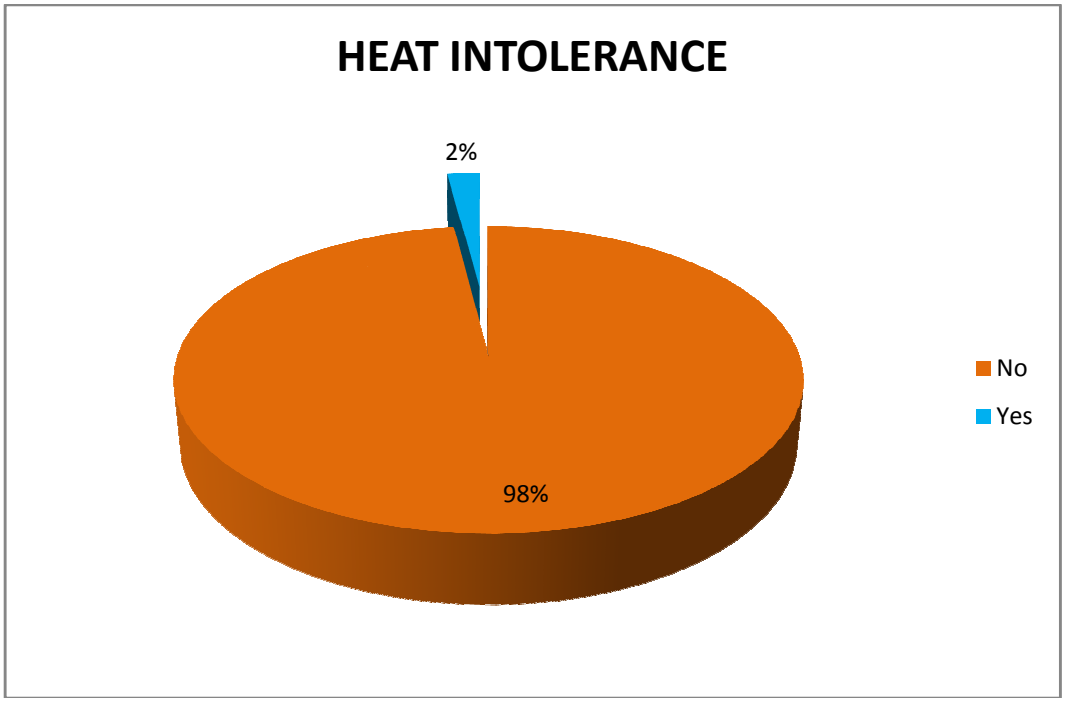
		Frequency	Percent
Valid	No	87	87.0
	Yes	13	13.0
	Total	100	100.0



In our study 13 (13%) patients of SLE were found to have weight loss.

HEAT INTOLERANCE

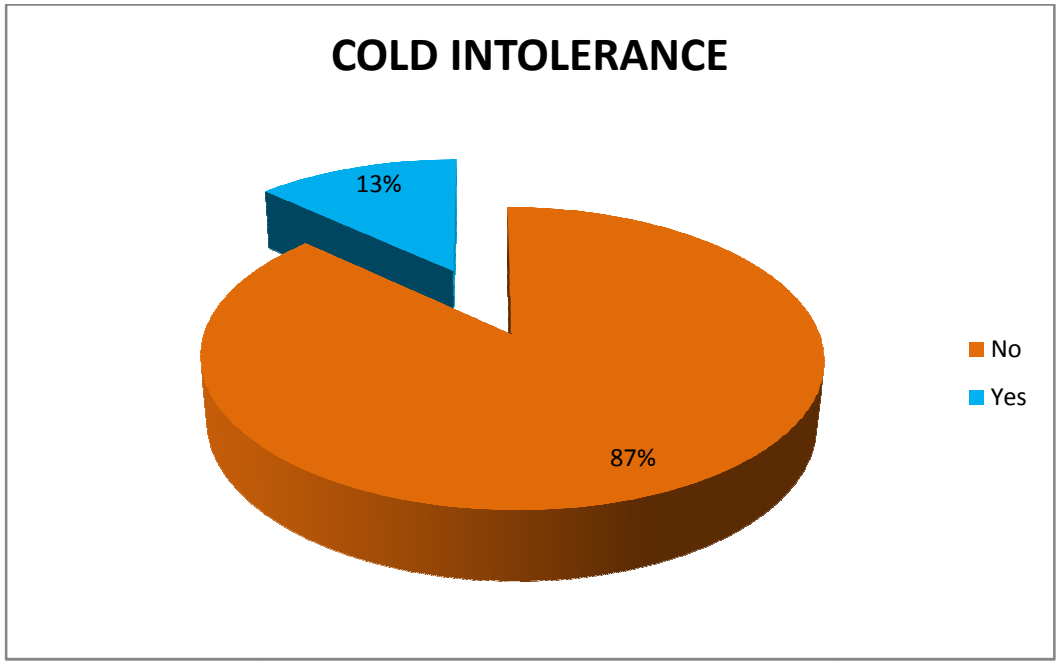
		Frequency	Percent
Valid	No	98	98.0
	Yes	2	2.0
	Total	100	100.0



Out of 100 patients of SLE, heat intolerance was seen in 2 (2%) patients .

COLD INTOLERANCE

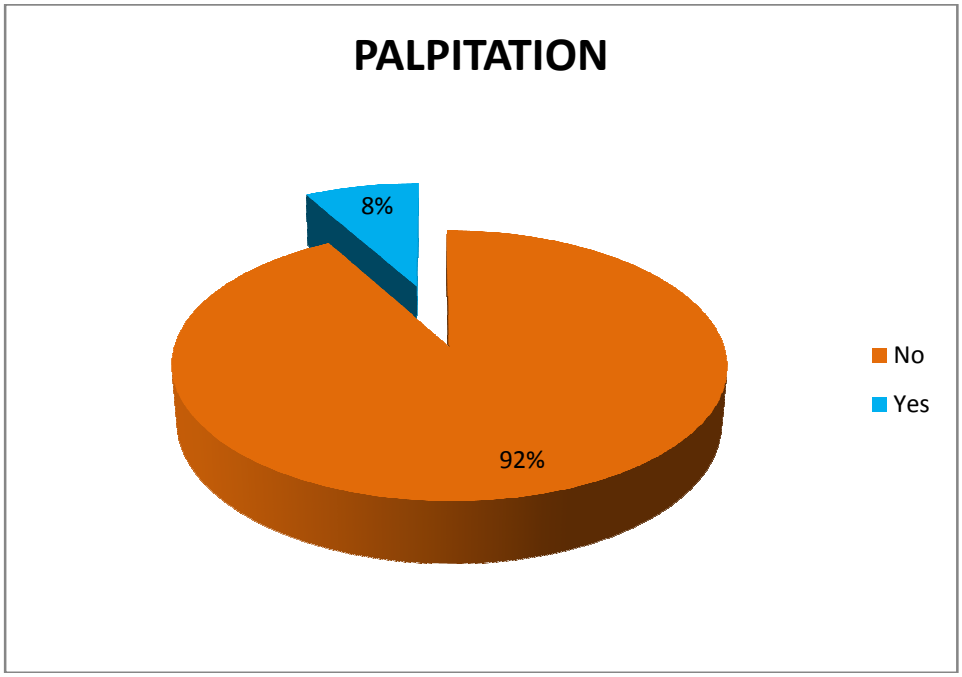
		Frequency	Percent
Valid	No	87	87.0
	Yes	13	13.0
	Total	100	100.0



In our study, cold intolerance was present in 13 (13%) patients of SLE.

PALPITATION

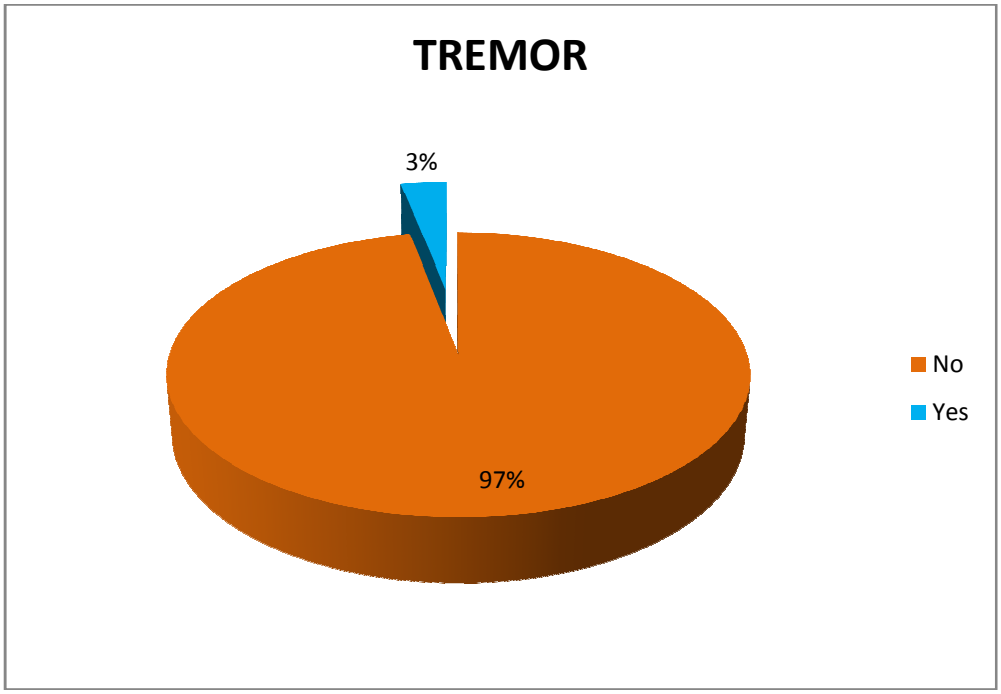
		Frequency	Percent	
Valid	No	92	92.0	
	Yes	8	8.0	
	Total	100	100.0	100.0



Among 100 patients of SLE, palpitation was seen in 8 (8%) patients .

TREMOR

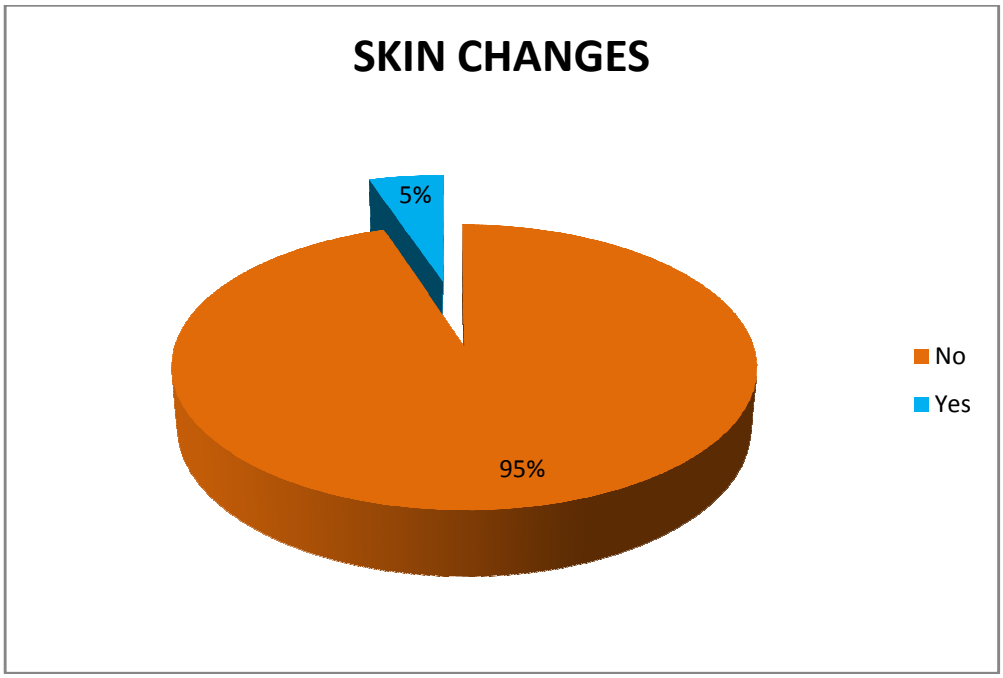
		Frequency	Percent
Valid	No	97	97.0
	Yes	3	3.0
	Total	100	100.0



Out of 100 SLE patients, tremor was observed in 3 (3%) patients.

SKIN CHANGES

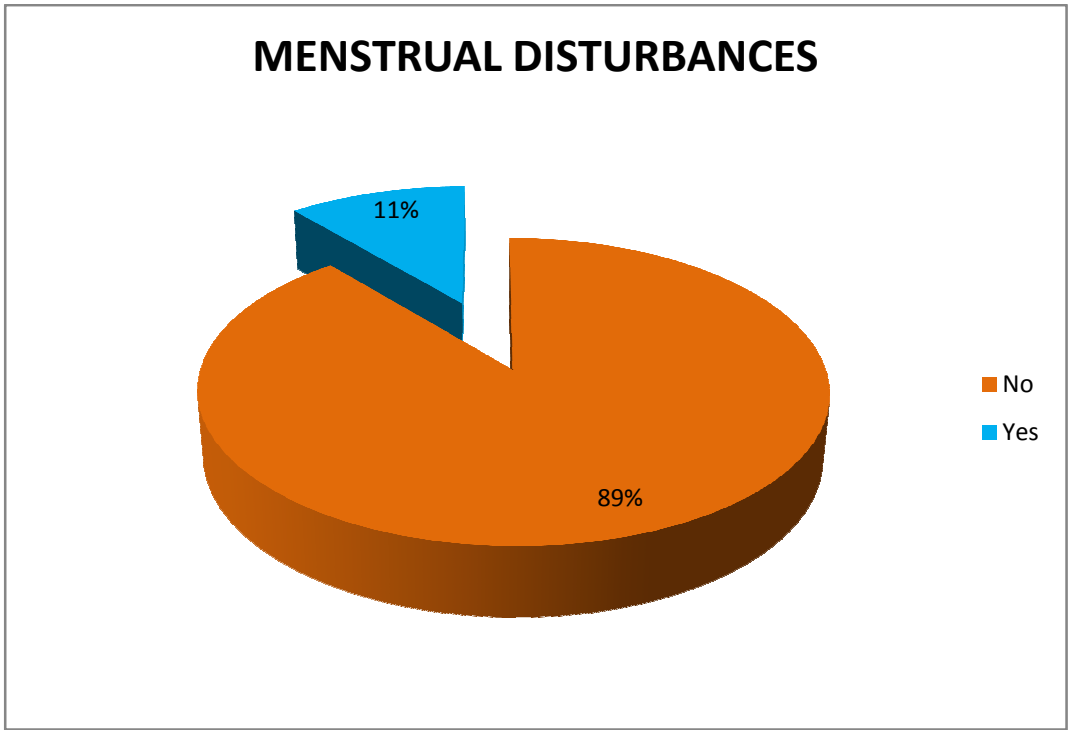
		Frequency	Percent
Valid	No	95	95.0
	Yes	5	5.0
	Total	100	100.0



In our study, skin manifestations was present in 5 (5%) patients.

MENSTRUAL DISTURBANCES

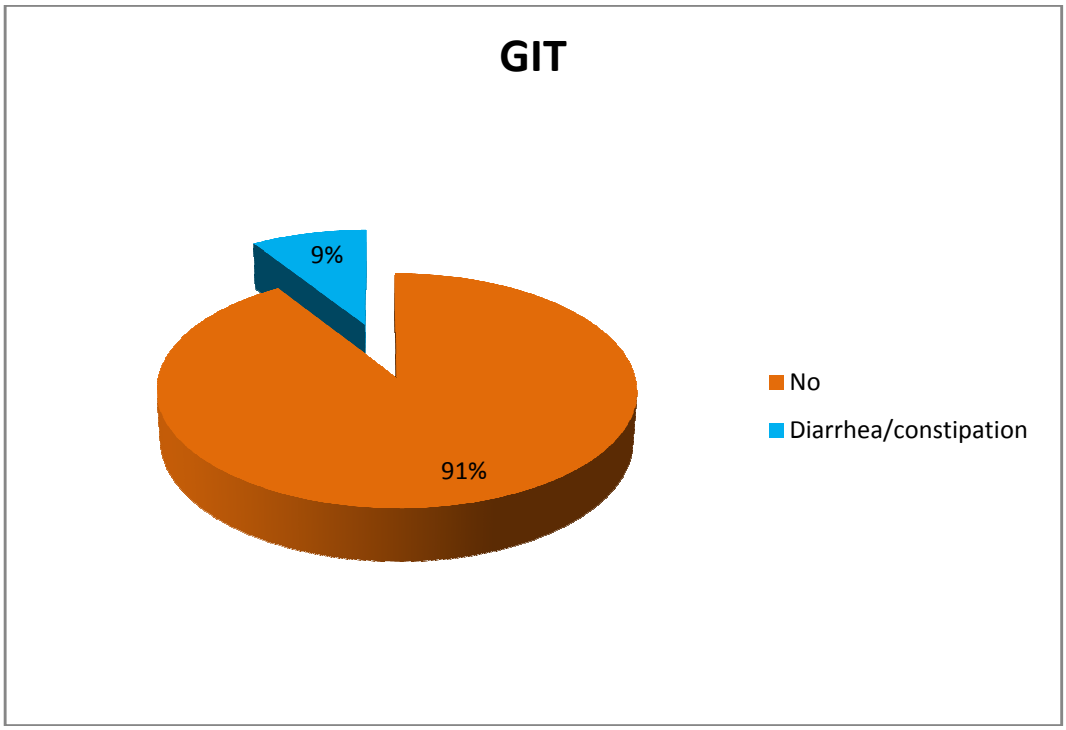
		Frequency	Percent
Valid	No	89	89.0
	Yes	11	11.0
	Total	100	100.0



Out of 100 patients of SLE , menstrual disturbances was found in 11 (11%) patients .

GIT

		Frequency	Percent
Valid	No	91	91.0
	Diarrhea/constipation	9	9.0
	Total	100	100.0



In our study, GIT disturbances like diarrhea and constipation was present in 9 (9%) patients.

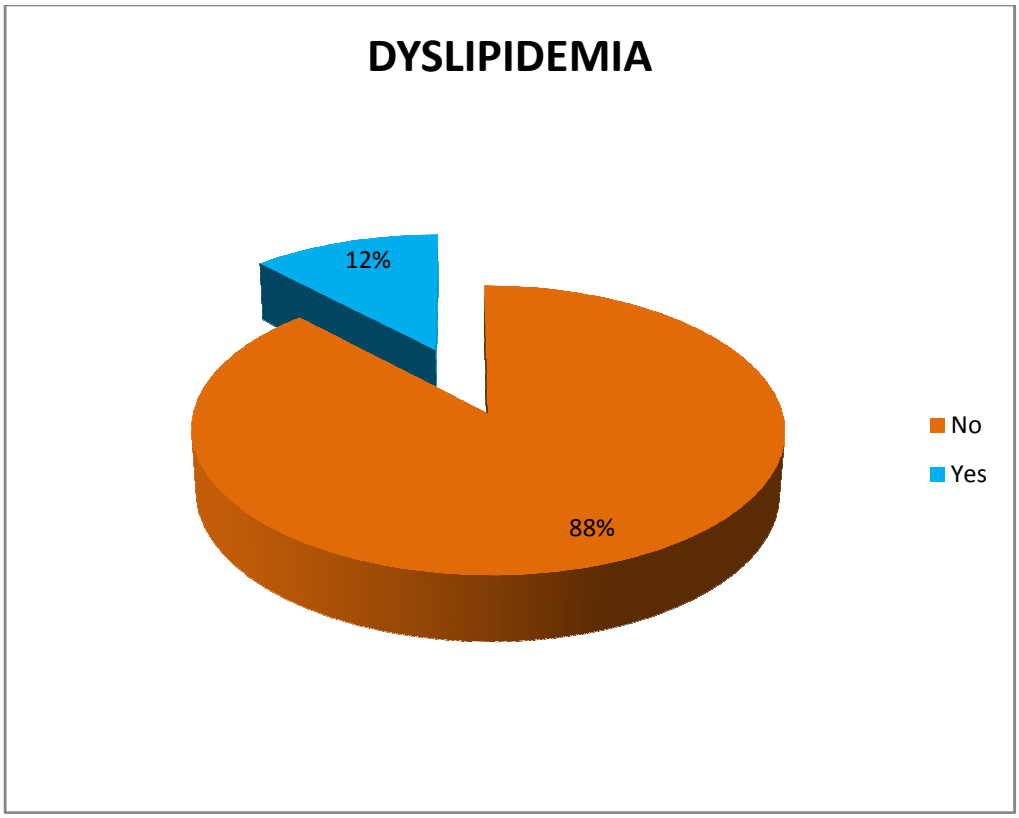
PSYCHIATRIC MANIFESTATION

		Frequency	Percent
Valid	No	93	93.0
	Yes	7	7.0
	Total	100	100.0

Out of 100 patients of SLE, psychiatric manifestations mainly depression was seen in 7 (7%) patients.

DYSLIPIDEMIA

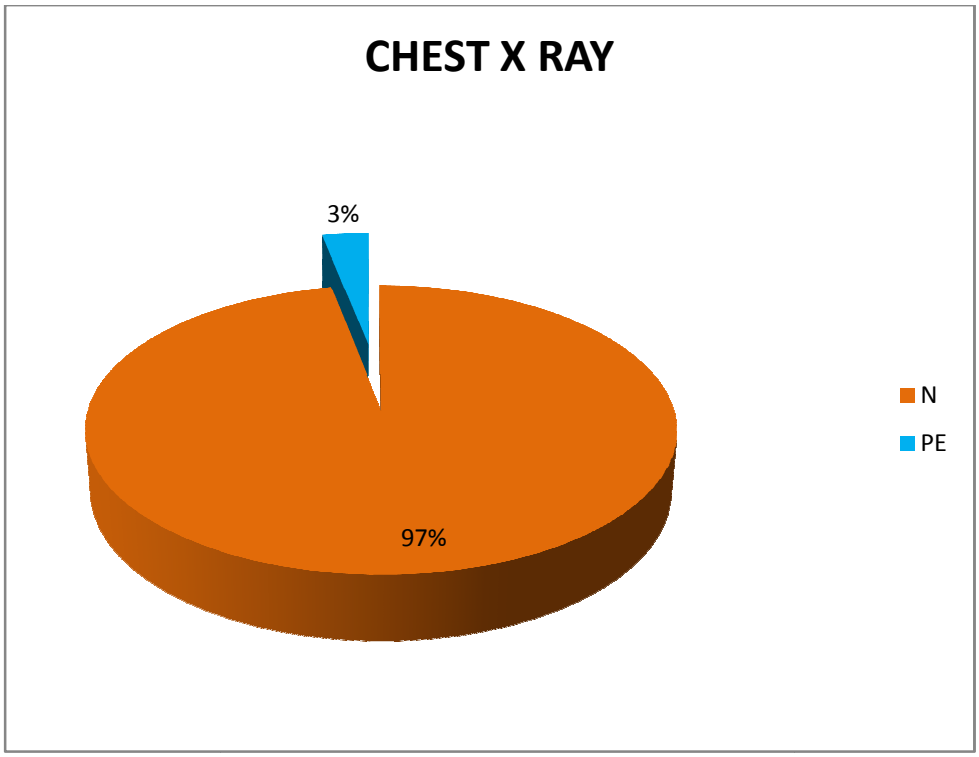
		Frequency	Percent
Valid	No	88	88.0
	Yes	12	12.0
	Total	100	100.0



In our study, 12 (12%) patients of SLE had dyslipidemia.

CHEST XRAY

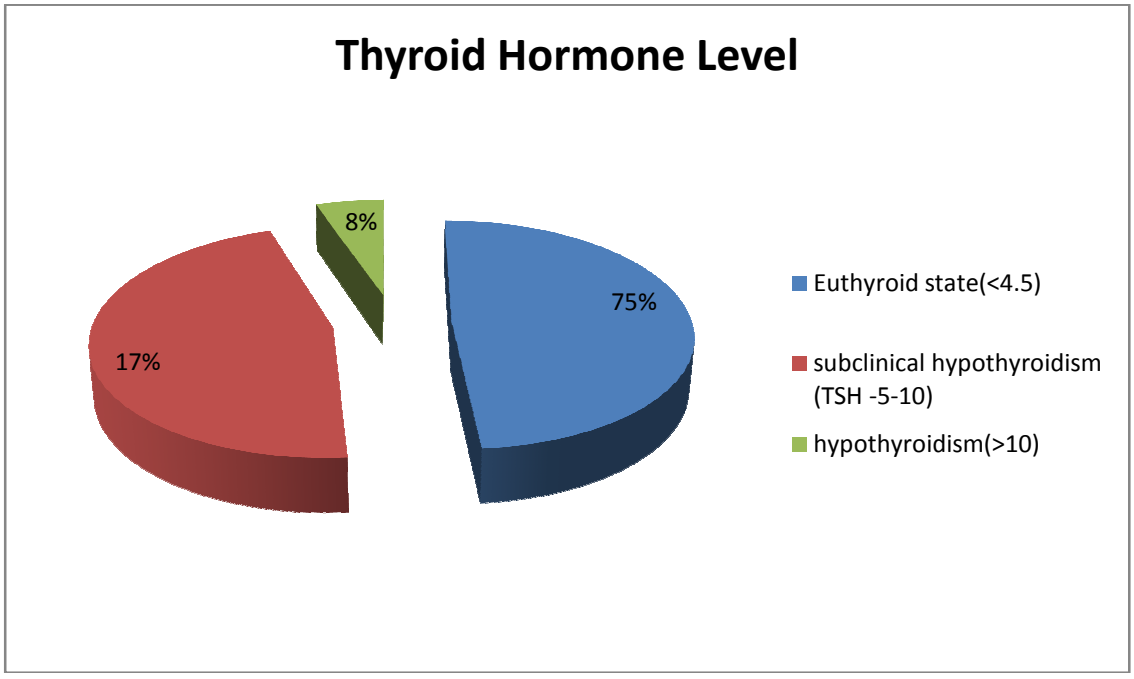
		Frequency	Percent
Valid	N	97	97.0
	PE	3	3.0
	Total	100	100.0



Among 100 patients of SLE, pleural effusion in Chest X-ray was present in 3 (3%) patients.

THYROID HORMONE LEVEL

		Frequency	Percent
Valid	Euthyroid state(<4.5)	75	75.0
	subclinical hypothyroidism (TSH -5-10)	17	17.0
	hypothyroidism(>10)	8	8.0
	Total	100	100.0



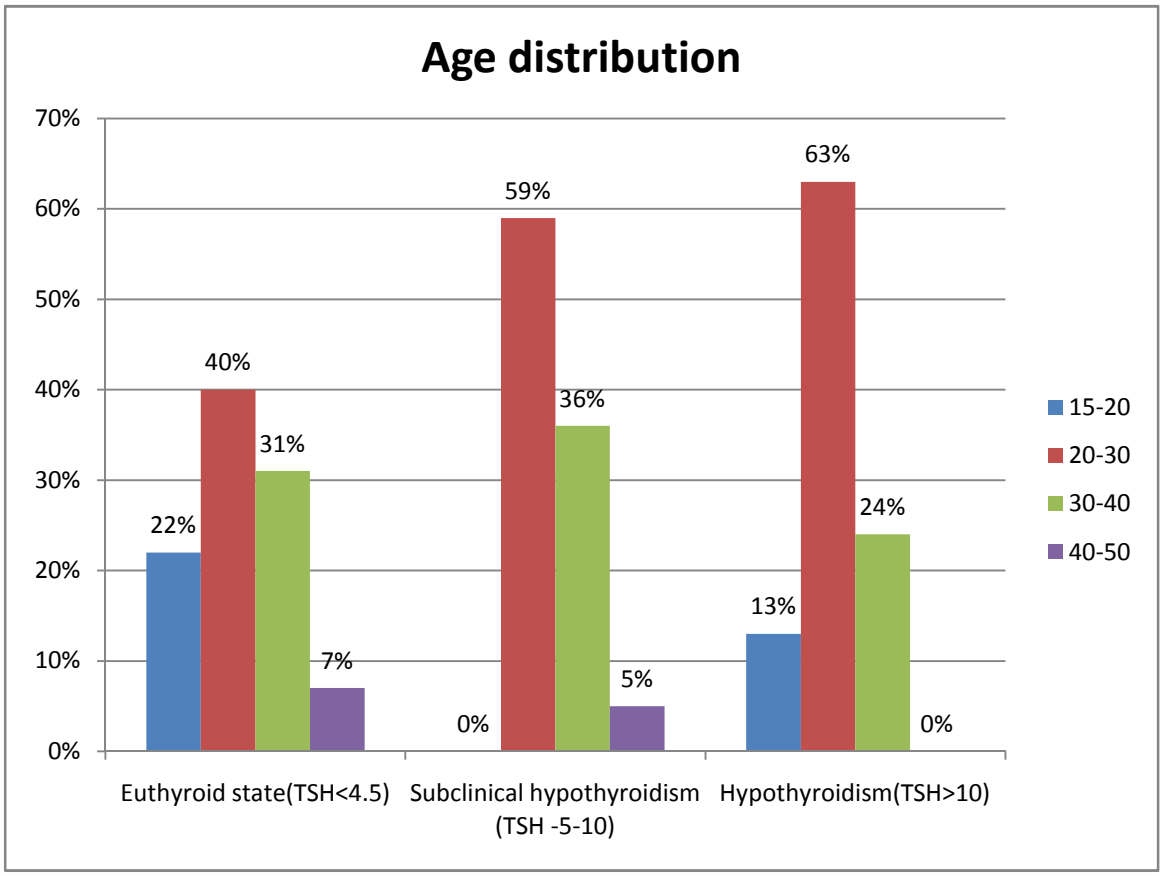
Among 100 patients of SLE, 8 (8%) patients were found to have overt hypothyroidism, 17 (17%) patients have subclinical hypothyroidism and 75 (75%) patients were in euthyroid state.

RESULTS

AGE GROUP - CROSS TABULATION

			THYROID			Total
			Euthyroid state(TSH< 4.5)	Subclinical hypothyroidism (TSH -5-10)	Hypothyroidism (TSH>10)	
age_group	15-20	Count	17	0	1	18
		% within THYROID	22.7%	0.0%	12.5%	18.0%
	20-30	Count	30	10	5	45
		% within THYROID	40.0%	58.8%	62.5%	45.0%
	30-40	Count	23	6	2	31
		% within THYROID	30.7%	35.3%	25.0%	31.0%
	40-50	Count	5	1	0	6
		% within THYROID	6.7%	5.9%	0.0%	6.0%
Total		Count	75	17	8	100
		% within THYROID	100.0%	100.0%	100.0%	100.0%

Pearson Chi-Square = 6.598 P>0.05

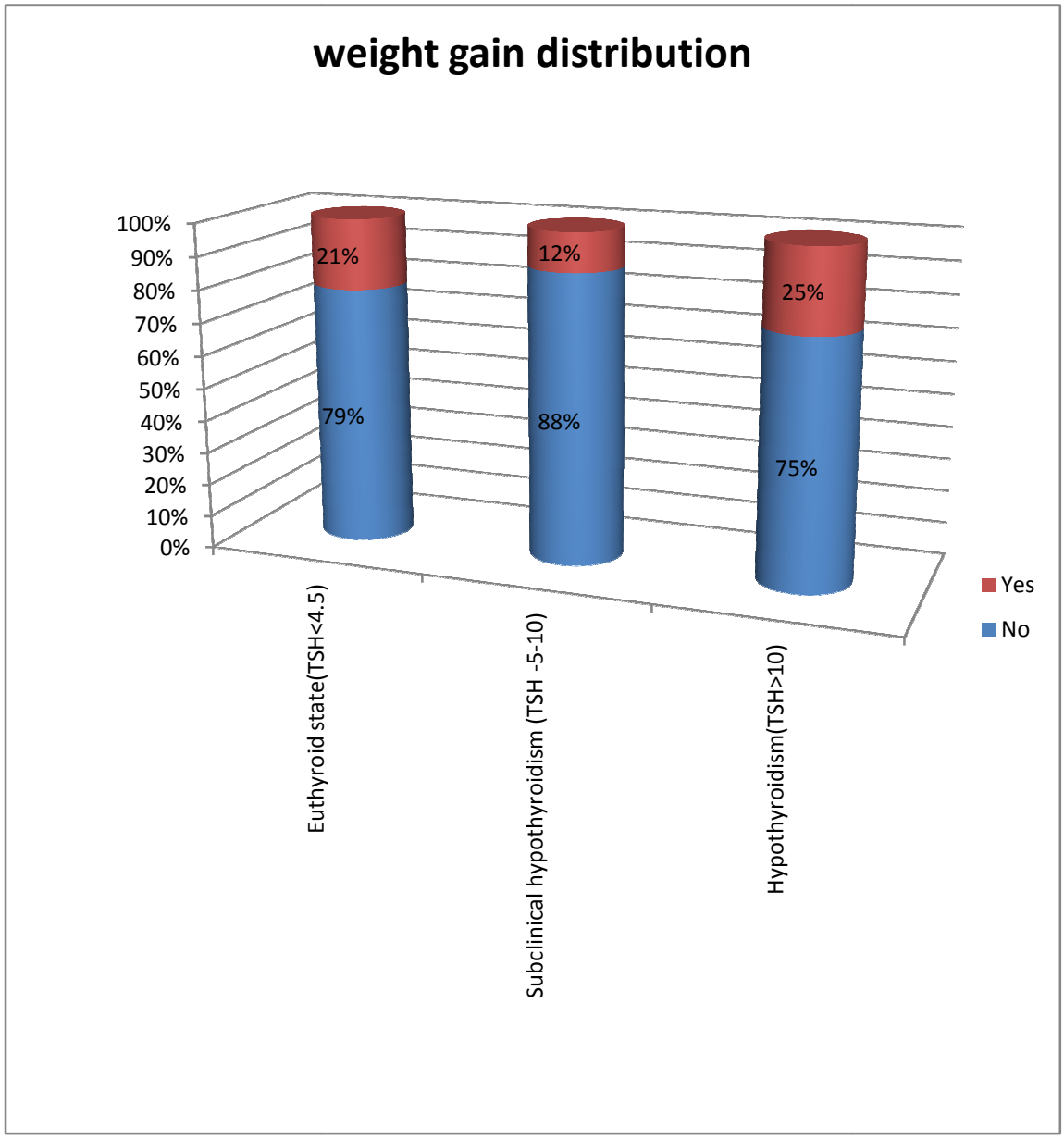

Age distribution
70%
60%
50%
40%
30%
20%
10%
0%
22%
40%
31%
7%
0%
59%
36%
5%
13%
63%
24%
0%
Euthyroid state(TSH<4.5)
Subclinical hypothyroidism (TSH -5-10)
Hypothyroidism(TSH>10)
15-20
20-30
30-40
40-50

CORRELATION BETWEEN WEIGHT GAIN AND THYROID DYSFUNCTION IN SLE PATIENTS

WEIGHT GAIN CROSS TABULATION :

			THYROID			Total
			euthyroid state(<4.5)	subclinical hypothyroidism (TSH -5-10)	hypothyroidism(>10)	
WEIGHT GAIN	No	Count	59	15	6	80
		% within THYROID	78.7%	88.2%	75.0%	80.0%
	Yes	Count	16	2	2	20
		% within THYROID	21.3%	11.8%	25.0%	20.0%
Total		Count	75	17	8	100
		% within THYROID	100.0%	100.0%	100.0%	100.0%

Pearson Chi-Square =0.929 P>0.05



In our study, weight gain was observed in 21 % of patients in euthyroid state, 12% of cases in subclinical hypothyroidism and 25 % patients of overt hypothyroidism which was stastically insignificant with p-value 0.929.

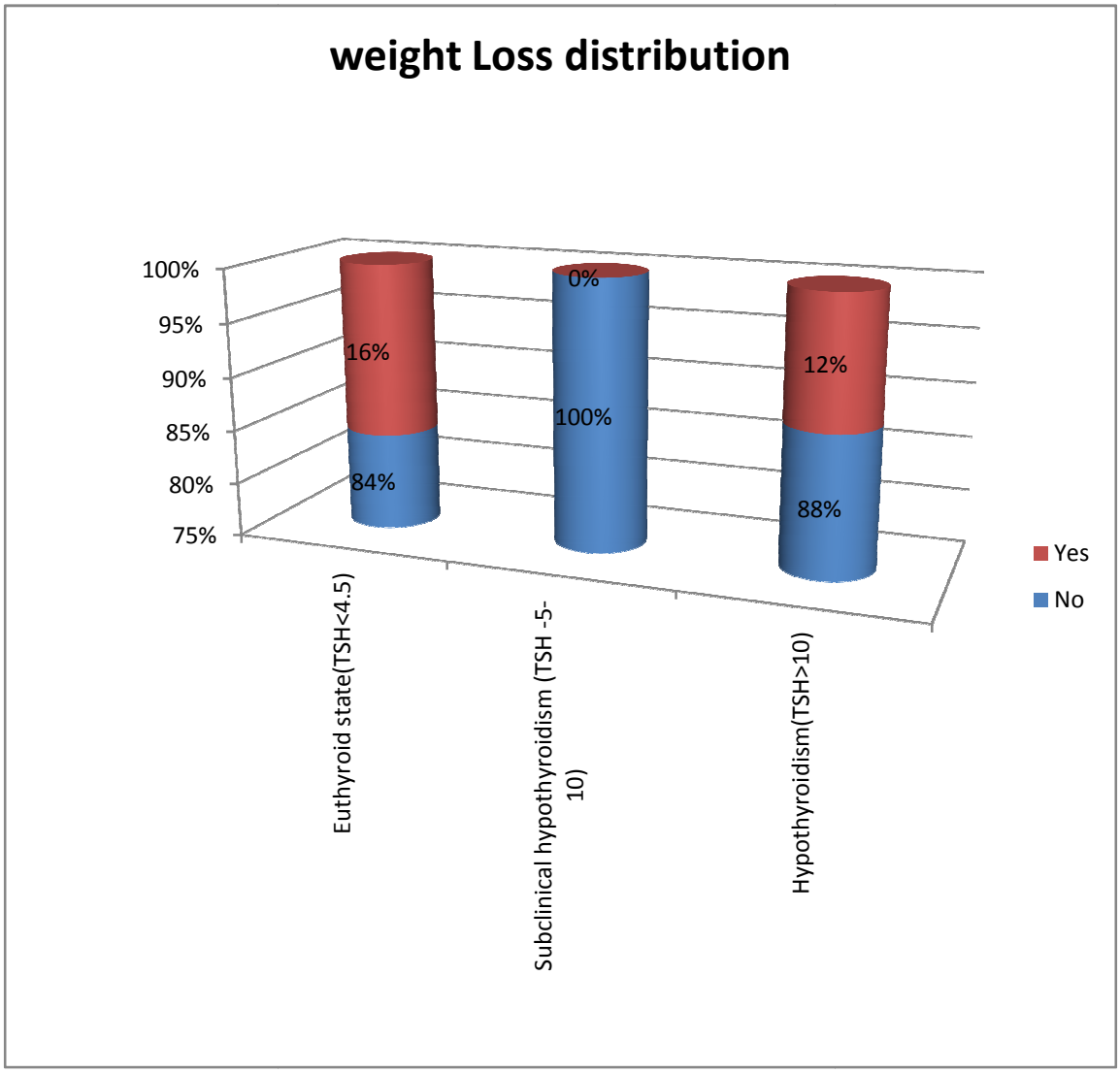
CORRELATION BETWEEN WEIGHT LOSS AND THYROID DYSFUNCTION IN SLE PATIENTS

WEIGHT LOSS

Crosstab

			THYROID			Total
			TSH <4.5	TSH 4.5-10	TSH >10	
WEIGHT LOSS	No	Count	63	17	7	87
		% within THYROID	84.0%	100.0%	87.5%	87.0%
	Yes	Count	12	0	1	13
		% within THYROID	16.0%	0.0%	12.5%	13.0%
Total		Count	75	17	8	100
		% within THYROID	100.0%	100.0%	100.0%	100.0 %

Pearson Chi-Square =3.139 P>0.05 (0.208)



In our study, the correlation between weight loss and thyroid dysfunction was observed. It was found to have 16% of patients in euthyroid state, 12% of patients in overt hypothyroidism and was not present in subclinical hypothyroidism which was not stastically significant with p-value 0.208.

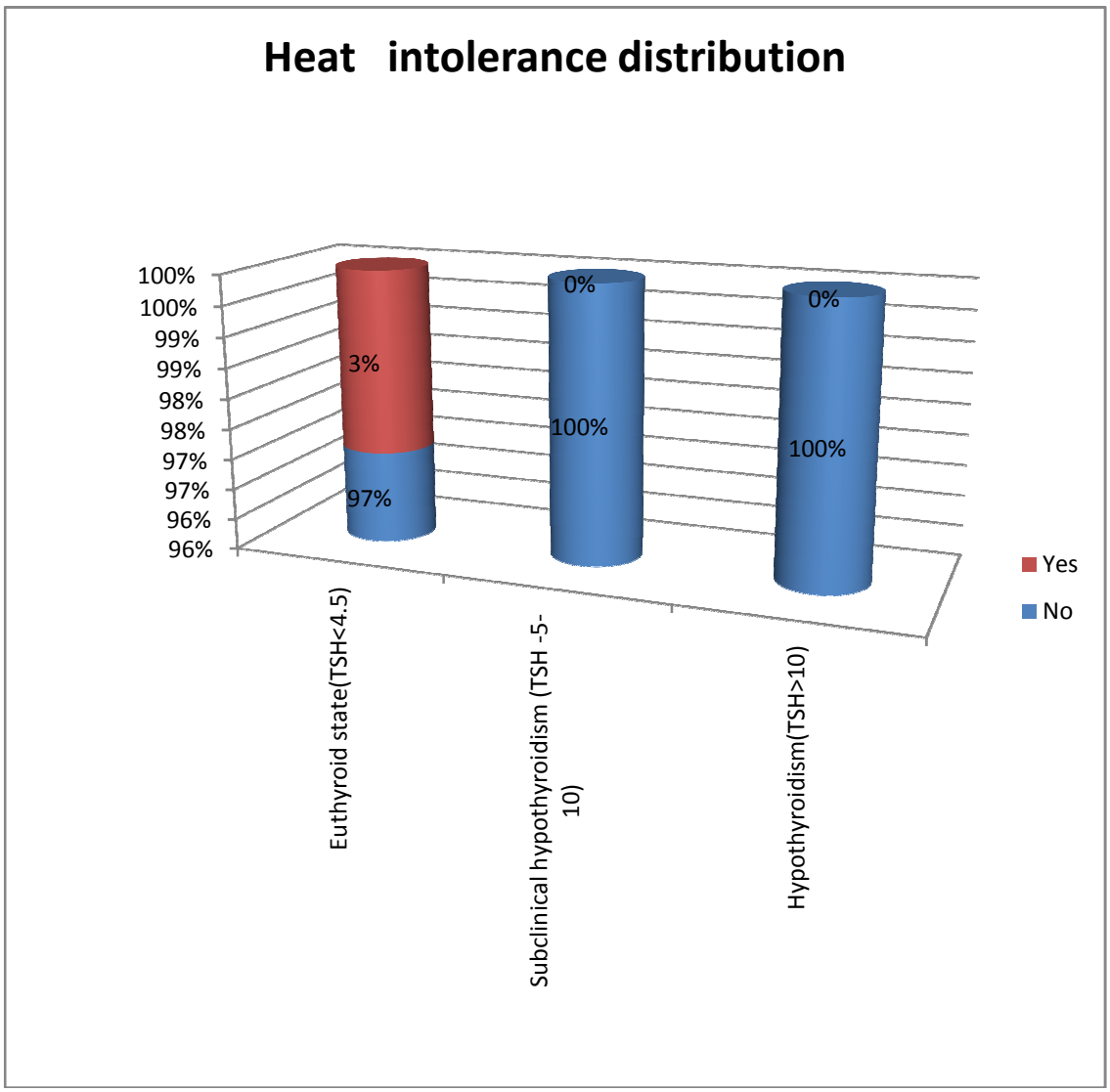
CORRELATION BETWEEN HEAT INTOLERANCE AND THYROID DYSFUNCTION IN PATEINTS WITH SLE

HEAT INTOLERANCE

Crosstab

			THYROID			Total
			TSH <4.5	TSH 4.5-10	TSH >10	
HEAT INTOLERANCE	No	Count	73	17	8	98
		% within THYROID	97.3%	100.0%	100.0%	98.0%
	Yes	Count	2	0	0	2
		% within THYROID	2.7%	0.0%	0.0%	2.0%
Total		Count	75	17	8	100
		% within THYROID	100.0%	100.0%	100.0%	100.0%

Pearson Chi-Square =0.680 P>0.05(0.712)



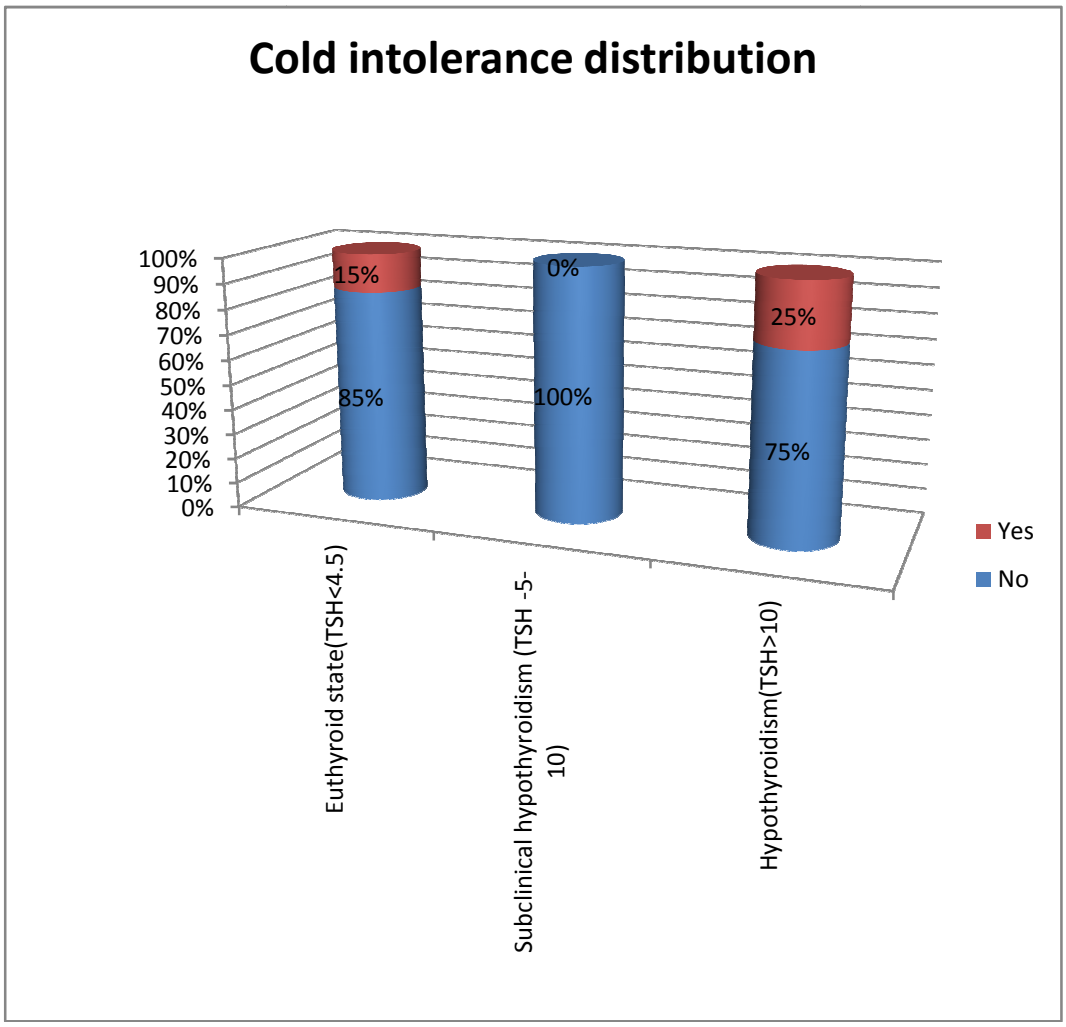
In our study, the presence of heat intolerance was observed in patients with thyroid disorder. It was found that there was no significant correlation between heat intolerance and thyroid dysfunction.

CORRELATION BETWEEN COLD INTOLERANCE AND THYROID DYSFUNCTION IN PATEINTS WITH SLE

Cross tabulation

			THYROID			Total
			euthyroid state(<4.5)	**subclinical hypothyroidism (TSH -5-10)**	**hypothyroidism(>10)**	
COLD INTOLERANCE	No	Count	64	17	6	87
		% within THYROID	85.3%	100.0%	75.0%	87.0%
	Yes	Count	11	0	2	13
		% within THYROID	14.7%	0.0%	25.0%	13.0%
Total		Count	75	17	8	100
		% within THYROID	100.0%	100.0%	100.0%	100.0%

Pearson Chi-Square =3.743 P>0.05



In our study, cold intolerance was seen in 15% of patients in euthyroid state and 25 % of patients with overt hypothyroidism which was stastically insignificant with p-value >0.05 .

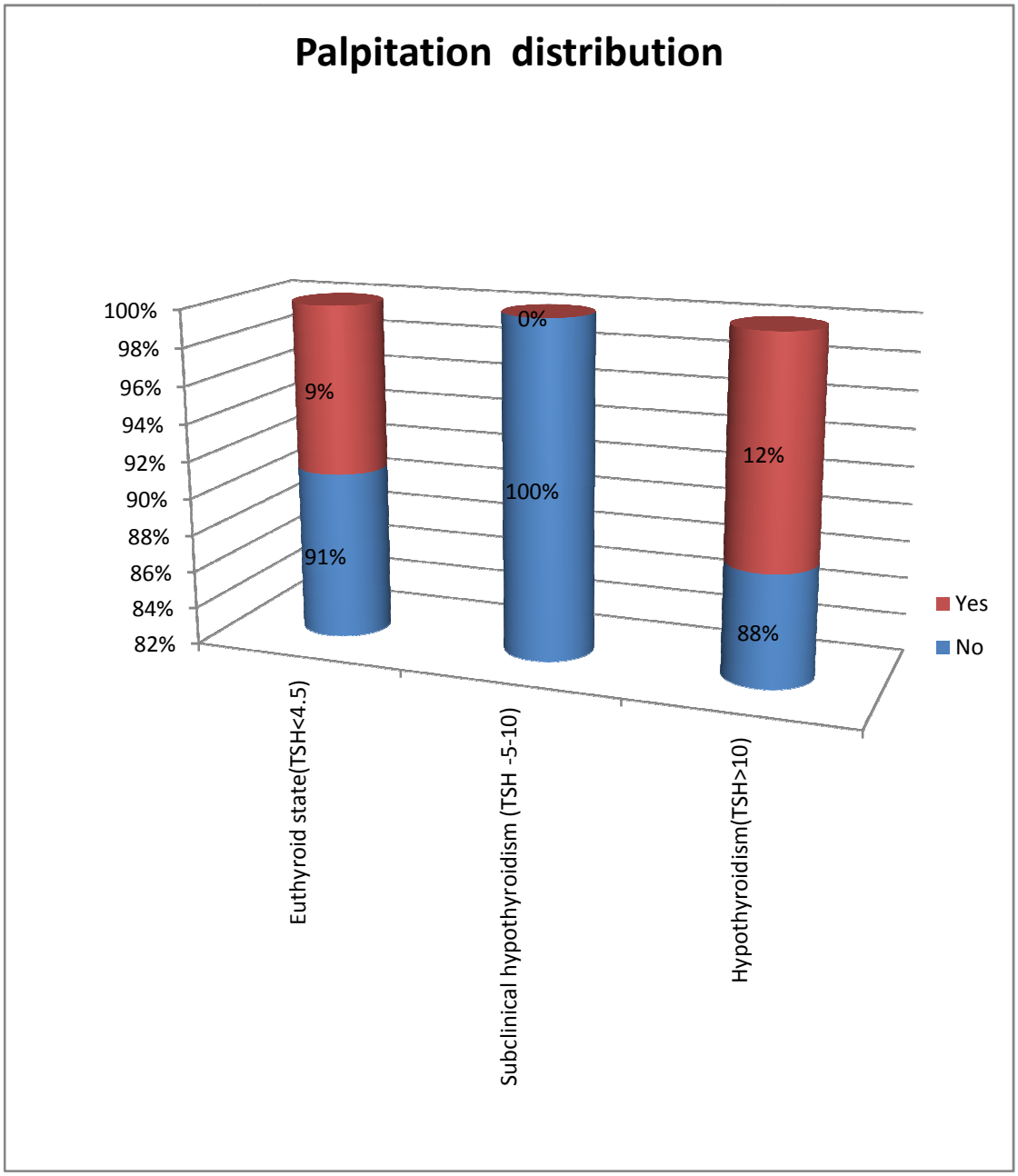
CORRELATION BETWEEN PALPITATION AND THYROID DYSFUNCTION IN PATEINTS WITH SLE

PALPITATION

Crosstab

			THYROID			Total
			TSH <4.5	TSH 4.5-10	TSH >10	
PALPITATION	No	Count	68	17	7	92
		% within THYROID	90.7%	100.0%	87.5%	92.0%
	Yes	Count	7	0	1	8
		% within THYROID	9.3%	0.0%	12.5%	8.0%
Total		Count	75	17	8	100
		% within THYROID	100.0%	100.0%	100.0%	100.0%

Pearson Chi-Square =1.880 P>0.05 (0.391)



In our study, the presence of palpitation and thyroid dysfunction was found to have statically insignificant with p-value - 0.391 .

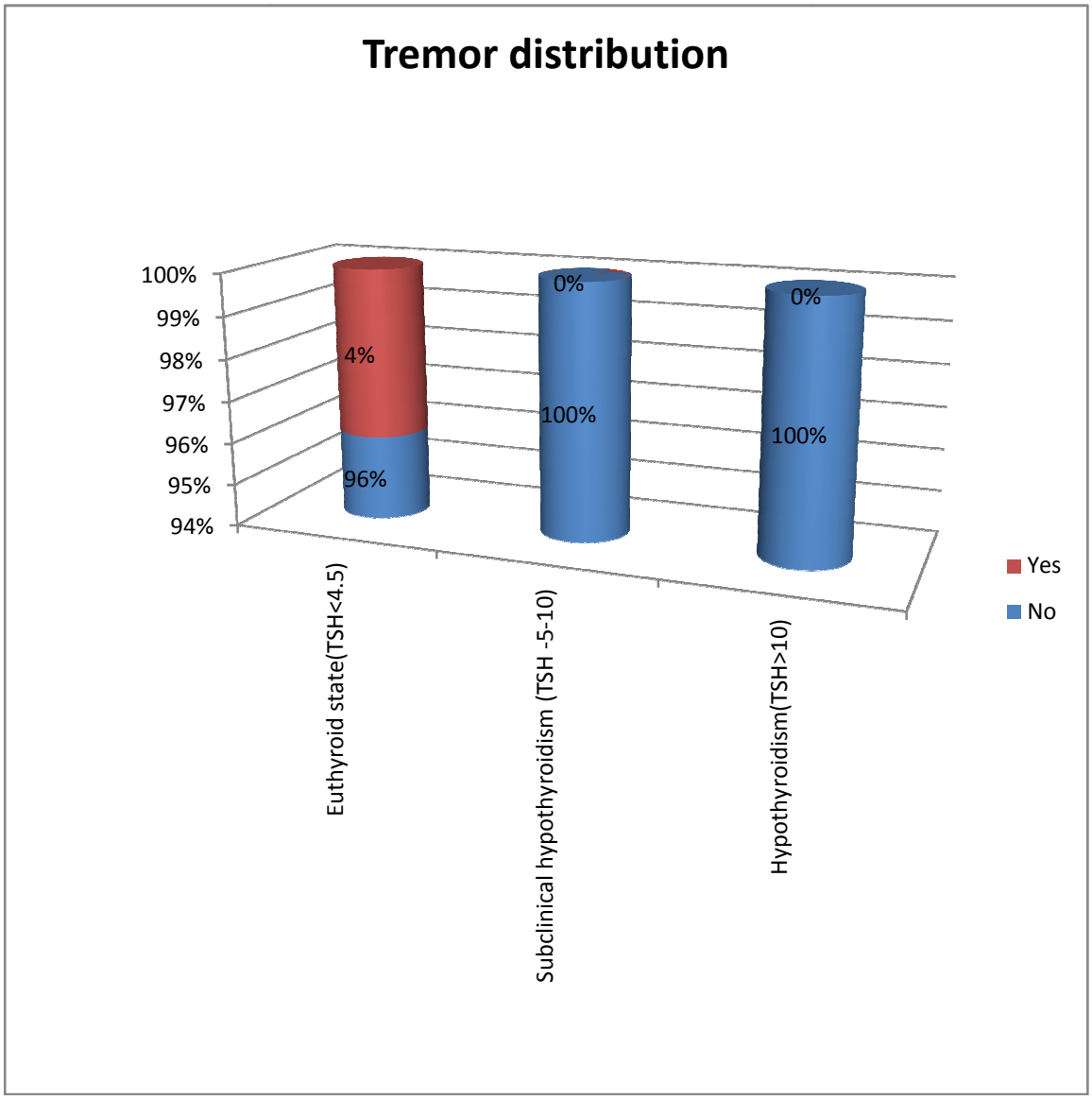
CORRELATION BETWEEN TREMOR AND THYROID DYSFUNCTION IN PATEINTS WITH SLE

TREMOR

Crosstab

			THYROID			Total
			TSH <4.5	TSH 4.5-10	TSH >10	
TREMOR	No	Count	72	17	8	97
		% within THYROID	96.0%	100.0%	100.0%	97.0%
	Yes	Count	3	0	0	3
		% within THYROID	4.0%	0.0%	0.0%	3.0%
Total		Count	75	17	8	100
		% within THYROID	100.0%	100.0%	100.0%	100.0%

Pearson Chi-Square =1.031 P>0.05(0.597)



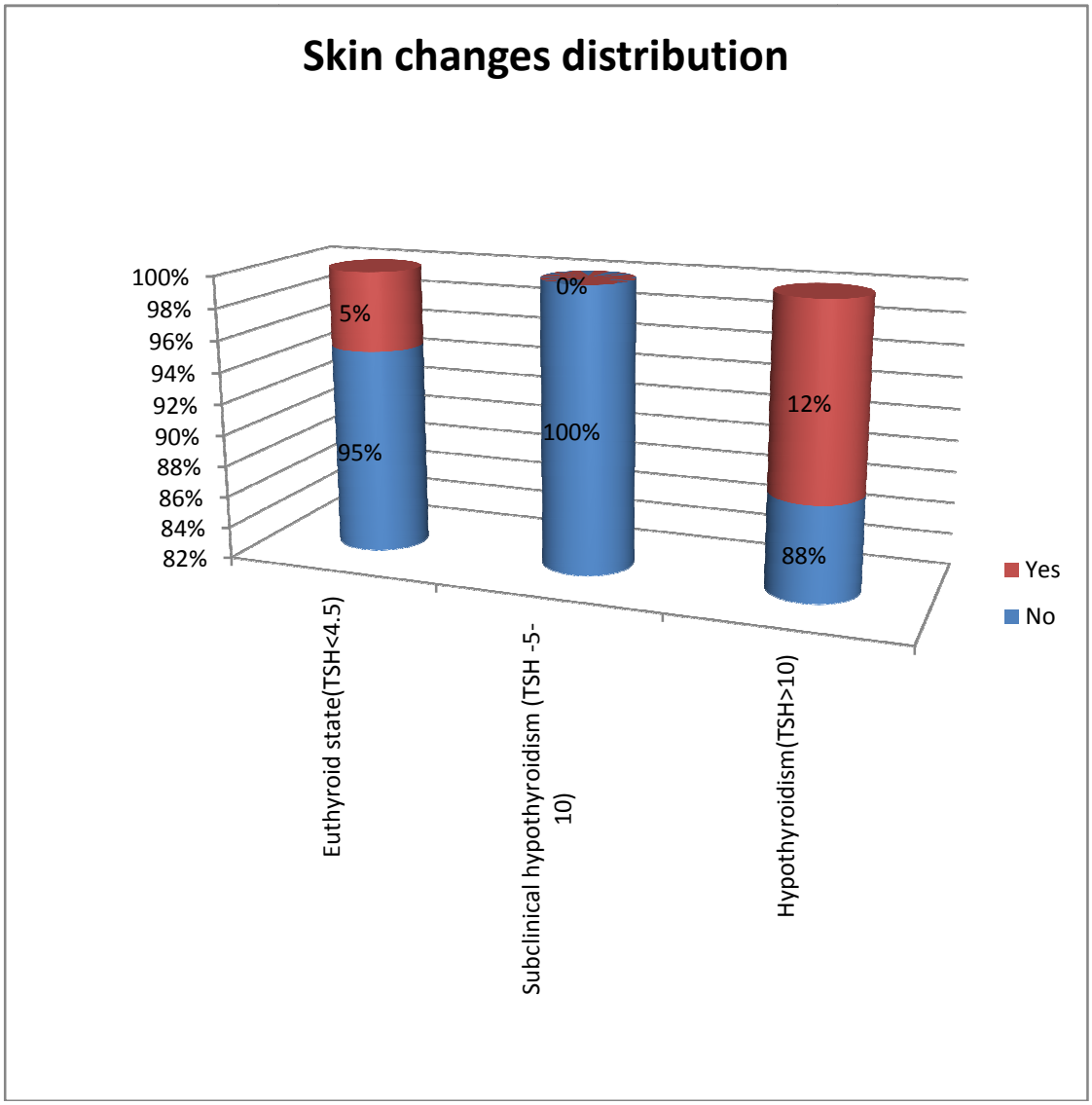
In our study, the correlation between tremor and thyroid dysfunction was observed and found to have statistically insignificant with p-value - 0.597

CORRELATION BETWEEN SKIN CHANGES AND THYROID DYSFUNCTION IN PATEINTS WITH SLE

Cross tabulation

			THYROID			Total
			euthyroid state(<4.5)	subclinical hypothyroidism (TSH -5-10)	hypothyroidism(>10)	
SKIN CHANGES	No	Count	71	17	7	95
		% within THYROID	94.7%	100.0%	87.5%	95.0%
	Yes	Count	4	0	1	5
		% within THYROID	5.3%	0.0%	12.5%	5.0%
Total		Count	75	17	8	100
		% within THYROID	100.0%	100.0%	100.0%	100.0%

Pearson Chi-Square =1.860 P>0.05



In our study, skin changes was observed in patients of SLE with thyroid dysfunction and it was present in 12% of patients with overt hypothyroidism with insignificant p-value >0.05

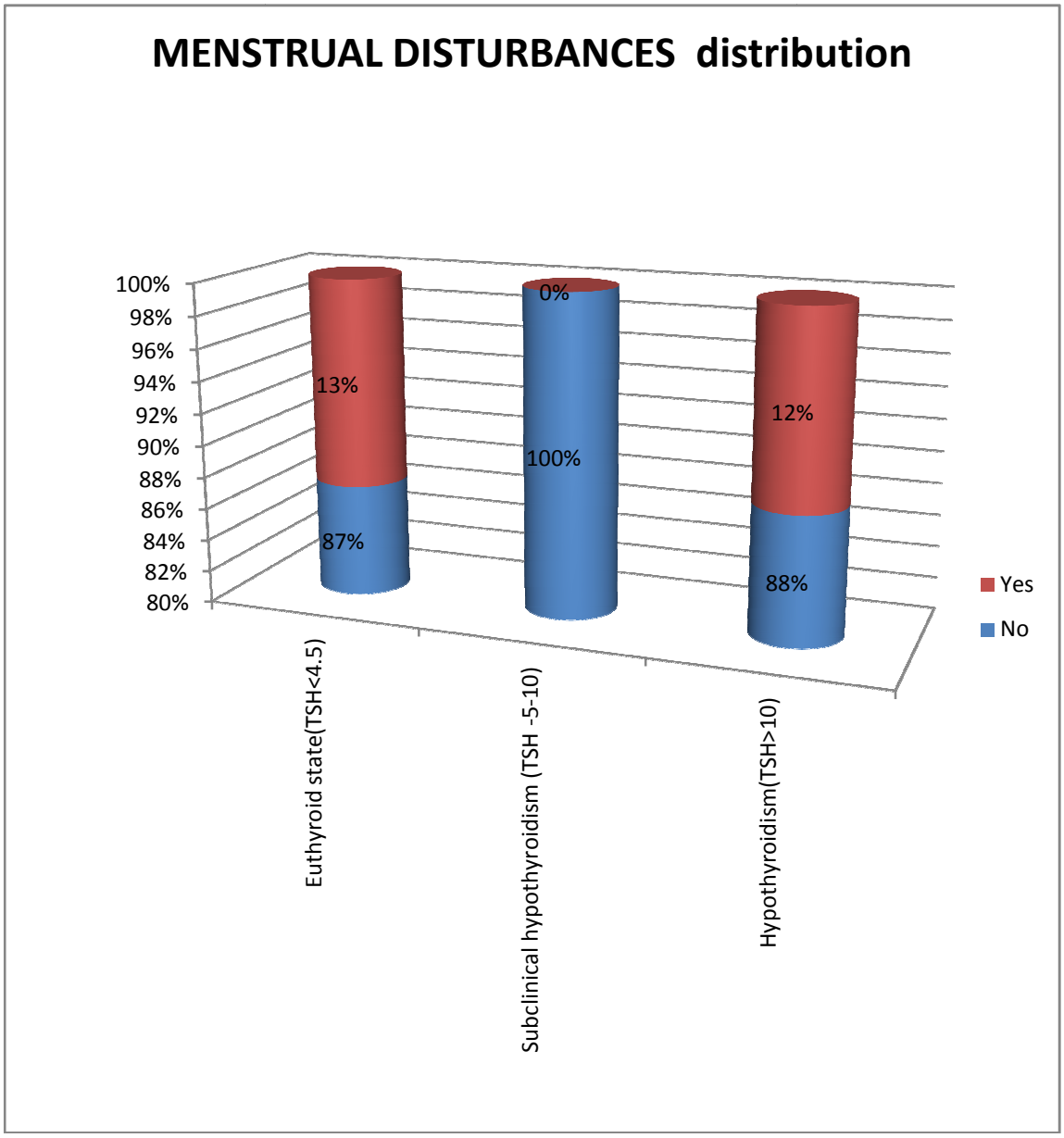
CORRELATION BETWEEN MENSTRUAL DISTURBANCES AND THYROID DYSFUNCTION IN PATEINTS WITH SLE

MENSTRUAL DISTURBANCES

Crosstab

			THYROID			Total
			TSH <4.5	TSH 4.5-10	TSH >10	
MENSTRUAL DISTURBANCES	No	Count	65	17	7	89
		% within THYROID	86.7%	100.0%	87.5%	89.0%
	Yes	Count	10	0	1	11
		% within THYROID	13.3%	0.0%	12.5%	11.0%
Total		Count	75	17	8	100
		% within THYROID	100.0%	100.0%	100.0%	100.0%

Pearson Chi-Square =2.537 P>0.05(0.281)



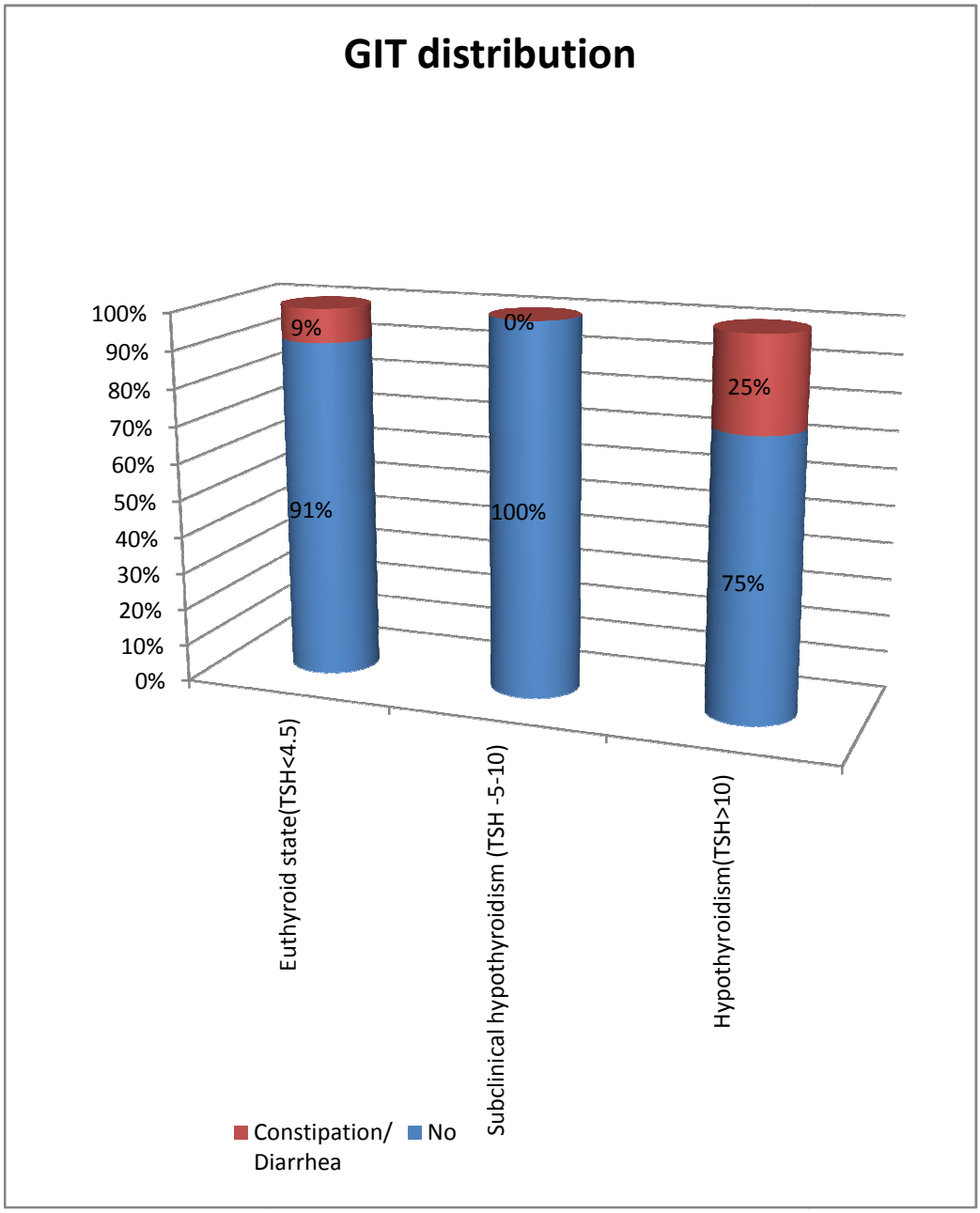
In our study, menstrual disturbances was equally distributed among patients of SLE with overt hypothyroidism and euthyroid state (12%) with insignificant p-value0.281 .

CORRELATION BETWEEN GIT DISTURBANCES AND THYROID DYSFUNCTION IN PATEINTS WITH SLE

GIT

Crosstab						
			THYROID			Total
			euthyroid state(<4.5)	subclinical hypothyroidism (TSH -5-10)	hypothyroidism(>10)	
GIT	No	Count	68	17	6	91
		% within THYROID	90.7%	100.0%	75.0%	91.0%
	Constipation/ Diarrhea	Count	7	0	2	9
		% within THYROID	9.3%	0.0%	25.0%	9.0%
Total		Count	75	17	8	100
		% within THYROID	100.0%	100.0%	100.0%	100.0%

Pearson Chi-Square =4.192 P>0.05



In our study, GIT disturbances was observed in 9% of patients with normal thyroid function and 25% of patients with overt hypothyroidism. It was found to have statically insignificant with p-value >0.05

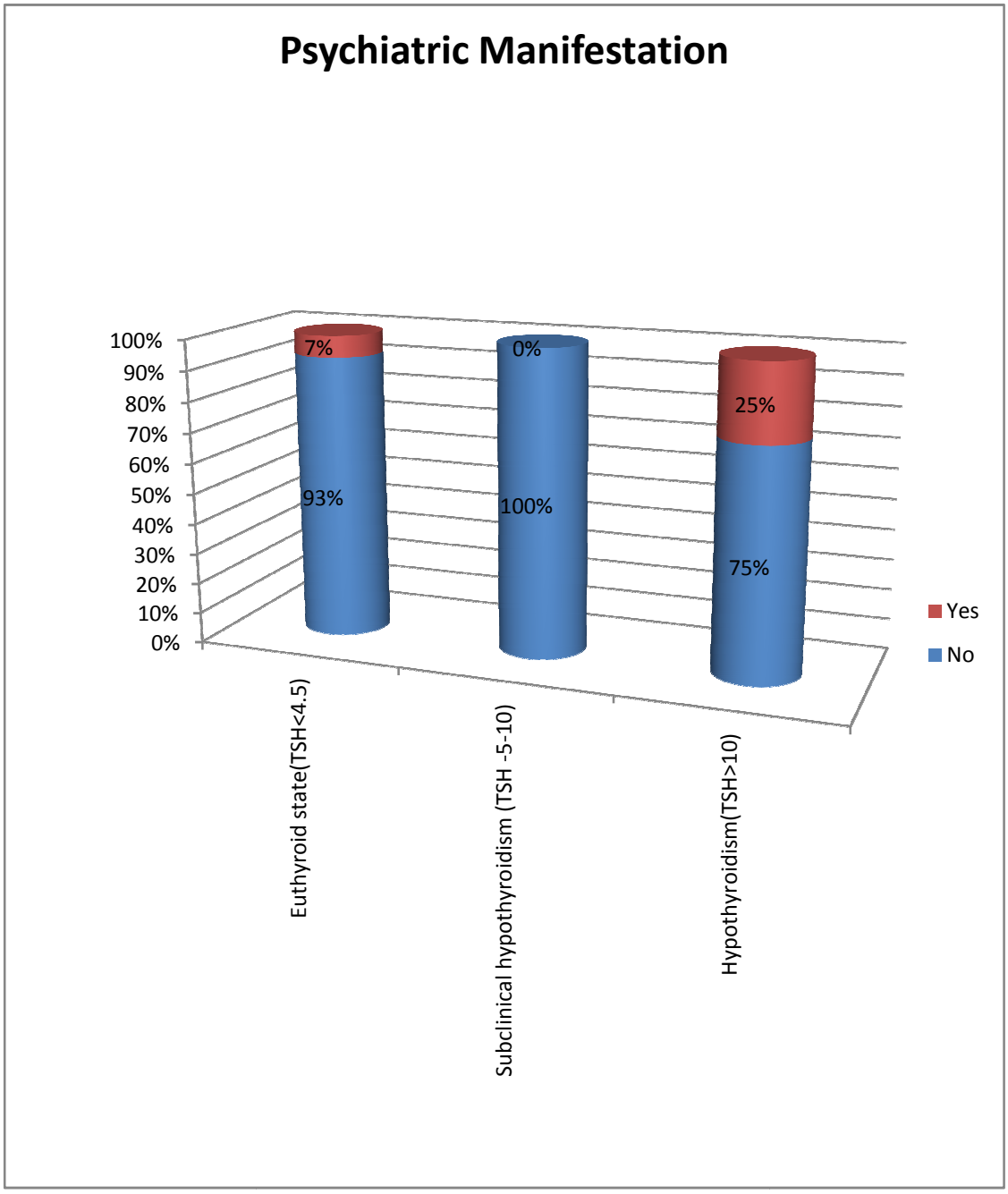
CORRELATION BETWEEN PSYCHIATRIC MANIFESTATIONS AND THYROID DYSFUNCTION IN PATEINTS WITH SLE

PSYCHIATRIC MANIFESTATION

Crosstab

			THYROID			Total
			TSH <4.5	TSH 4.5-10	TSH >10	
PSYCHIATRIC MANIFESTATION	No	Count	70	17	6	93
		% within THYROID	93.3%	100.0%	75.0%	93.0%
	Yes	Count	5	0	2	7
		% within THYROID	6.7%	0.0%	25.0%	7.0%
Total		Count	75	17	8	100
		% within THYROID	100.0%	100.0%	100.0%	100.0%

Pearson Chi-Square =5.274 P>0.05(0.072)



In our study, psychiatric manifestation was seen in 25% of cases of overt hypothyroidism and 7% of patients with normal thyroid function. It was found that there was no stastical significance with p-value 0.072.

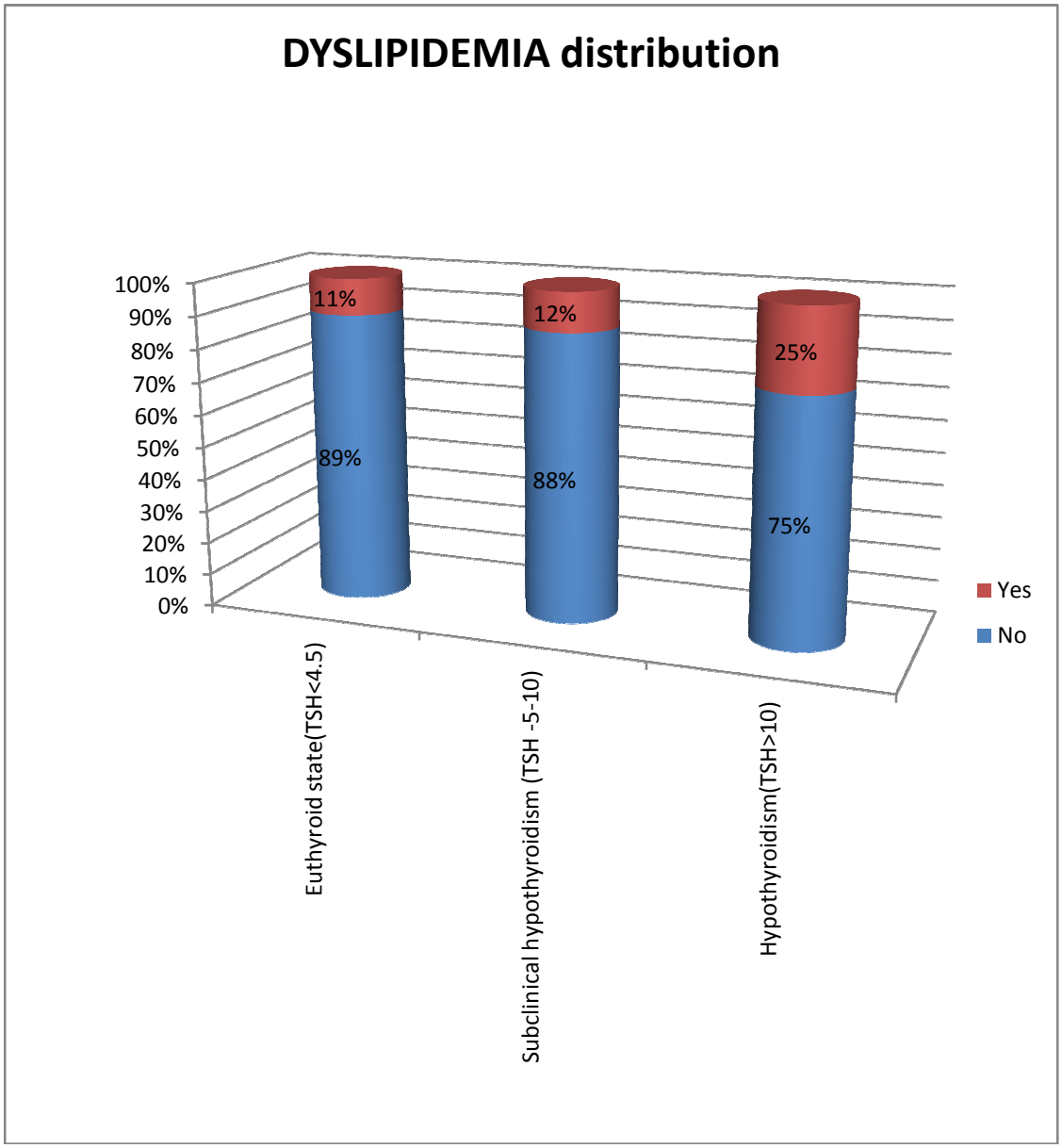
CORRELATION BETWEEN DYSLIPIDEMIA AND THYROID DYSFUNCTION IN PATEINTS WITH SLE

DYSLIPIDEMIA

Cross tabulation

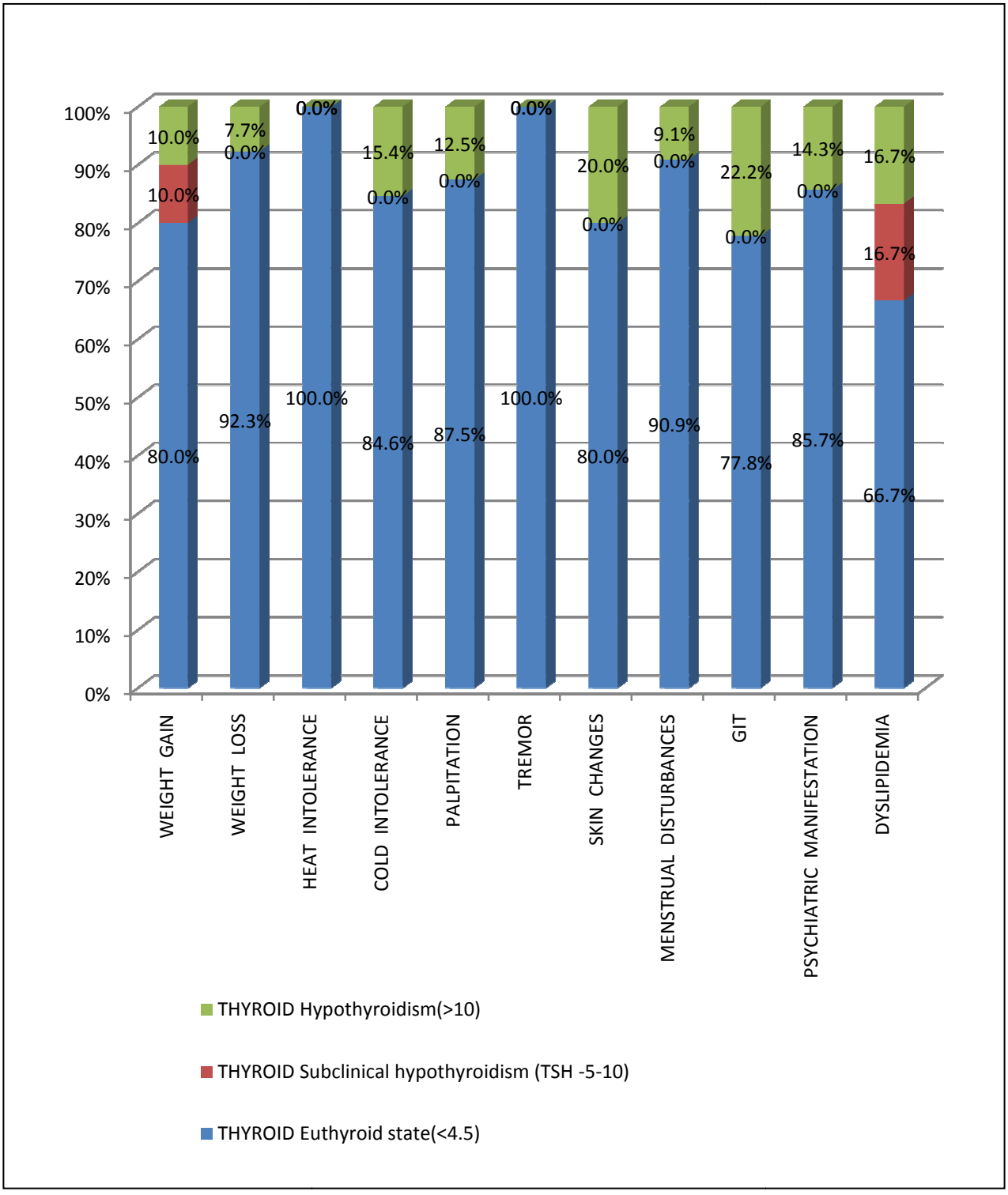
			THYROID			Total
			euthyroid state(<4.5)	**subclinical hypothyroidism (TSH -5-10)**	**hypothyroidism(>10)**	
DYSLIPIDEMIA	No	Count	67	15	6	88
		% within THYROID	89.3%	88.2%	75.0%	88.0%
	Yes	Count	8	2	2	12
		% within THYROID	10.7%	11.8%	25.0%	12.0%
Total		Count	75	17	8	100
		% within THYROID	100.0%	100.0%	100.0%	100.0%

Pearson Chi-Square =1.407 P>0.05



In our study, the occurence of dyslipidemia was seen in 25% of patients with overt hypothyroidism, 12% of patients with subclinical hypothyroidism and 11% cases of euthyroid state with insignificant p-value >0.05

PREVALENCE OF CLINICAL SYMPTOMS AMONG PATIENTS OF SLE WITH THYROID DYSFUNCTION



DISCUSSION

DISCUSSION

Our study was conducted in patients with SLE to know the prevalence of thyroid dysfunction. Our study population included 100 patients, those who are fitting into the diagnostic criteria of SLE assessed by clinical and biochemical evidence .All the 100 patients were evaluated and screened for the presence of thyroid dysfunction .Analysis was made to establish the correlation between the prevalence of thyroid dysfunction and its clinical correlation by using Chi-square test. Following were the observations made in our study with the patients of SLE .

Age distribution :

In 100 patients of SLE, majority cases of subclinical and clinical hypothyroidism were in the age group of 20 - 30 years adults .

Clinical features :

Weight Gain :

Out of 100 patients studied ,it was present in 16 (21%) cases of euthyroid patients , 2 (12%) cases of subclinical hypothyroidism and 2 (25%) cases of clinical hypothyroidism .

Weight Loss :

Among 100 patients, 12 (16%) patients of euthyroid and 13 (13%)patients of clinical hypothyroidism had weight loss . There is no significant weight loss observed in subclinical hypothyroidism.

Heat Intolerance :

In 100 patients of SLE, it was observed only in 2 (3%) patients of euthyroid and not observed in subclinical and clinical hypothyroidism.

Cold Intolerance :

Out of 100 patients studied, 11 (15%) cases of euthyroid had cold intolerance.

Palpitation :

Among 100 patients studied, palpitation was seen in 7(9%) patients of euthyroid and 1 (12%) patient of clinical hypothyroidism .

Tremor :

It was observed only in 3 (4%) patients of euthyroid patients , not observed in subclinical and clinical hypothyroidism .

Skin changes :

Out of 100 patients, it was seen in 12 (12.5%) patients of clinical hypothyroidism and 4 (5%) of SLE patients with normal thyroid functional status .

Menstrual Disturbances :

Out of 100 patients, menstrual disturbances was observed in 10 (13%) patients of euthyroid and 1(12%) patient of clinical hypothyroidism.

GIT Symptoms :

In our study, 7(9%) cases of euthyroid had diarrhea and constipation whereas 2(25%) patients of clinical hypothyroidism had GIT disturbances .

Psychiatric manifestations :

Among 100 patients studied, psychiatric manifestations was observed in 5(7%) patients of SLE without thyroid dysfunction and 2(25%) patients of clinical hypothyroidism .

Dyslipidemia :

It was present in 8(11%) patients of normal thyroid function whereas 2(25%) cases of subclinical and 2(12%) patients of clinical hypothyroidism .

THYROID DYSFUNCTION IN SLE :

Out of 100 patients in our study, 25 patients were found to have thyroid dysfunction. Most of the patients of SLE with thyroid dysfunction were clinically asymptomatic and symptoms are present even in patients with feuthyroid state .

In this study the prevalence of thyroid dysfunction and its clinical correlation was done among the 100 patients of SLE and this study was comparable to studies conducted by Kakehasi et al [46], Zakeri and Sandooghi [47] , Sahin et al [48].

It was observed that the prevalence of subclinical hypothyroidism was slightly higher in our study which was about 17%, followed by clinical hypothyroidism 8%. In our study no subclinical and clinical hyperthyroidism case was observed.

CONCLUSION

CONCLUSION

Following results were concluded from our study ;

- SLE was more commonly seen in females of child bearing age group in the third decade.
- The occurrence of weight gain was observed mainly in patients of SLE with euthyroid state and clinical hypothyroidism.
- The incidence of weight loss in our study was present equally among the patients of SLE with euthyroid and clinical hypothyroidism. It was not found in patients of subclinical hypothyroidism.
- There was no stastical significant correlation was observed between the presence of heat intolerance and thyroid dysfunction in patients with SLE
- Cold intolerance was not seen significantly in patients of SLE with thyroid dysfunction.
- It was observed that, the occurrence of palpitation was not significantly present among the patients of SLE with thyroid abnormalities.
- Tremor was noted only in few cases of euthyroid and not observed in patients with thyroid dysfunction.

- Skin manifestations were present in few cases of clinical hypothyroidism and it was not correlating significantly in patients with thyroid dysfunction.
- The presence of menstrual disturbances was distributed equally in patients of SLE with euthyroid state and clinical hypothyroidism
- Most of the patients with clinical hypothyroidism was found to have GIT disturbances mainly diarrhea and constipation.
- Among the patients of SLE with thyroid dysfunction the psychiatric manifestations are more commonly present in clinical hypothyroidism.
- In our study nearly quarter of the patients with subclinical hypothyroidism had dyslipidemia

In our study the symptoms are not correlating significantly and it was difficult to clinically detect the presence of thyroid dysfunction among patients with SLE because of the similarity of certain clinical symptoms which occurred both in SLE and thyroid disorder .

The prevalence of subclinical hypothyroidism and clinical hypothyroidism among patients in SLE was clinically significant.

The occurrence of subclinical and clinical hyperthyroidism was not significant in our study.

SUMMARY

SUMMARY

SLE is an autoimmune disorder of unknown aetiology affects any system of the body.

Development of thyroid dysfunction mainly autoimmune thyroiditis is more prevalent in SLE patients when compared to the general population. However this may be unnoticed because of the similarity of clinical manifestations between SLE and thyroid disorders .

The prevalence of thyroid dysfunction in patients with SLE is more common when compared to the general population. SLE patients with thyroid disorder are more prone for increased risk of cardiovascular disease because of accelerated atherosclerosis.

The cardiovascular risk is independent of lipid profile parameters.

The routine screening of patients with SLE for thyroid dysfunction is essential which helps in early detection and treatment of thyroid disorder.

BIBLIOGRAPHY

BIBLIOGRAPHY

1. Cohen-Solal JF, Jeganathan V, Hill L, et al: Hormonal regulation of B-cell function and systemic lupus erythematosus, 528–532, 2008.
2. Harley JB, Alarcon-Riquelme ME, Criswell LA, et al: Genome-wide association scan in women with systemic lupus erythematosus identifies susceptibility variants in ITGAM, PXK, KIAA1542 and other loci, 204–210, 2008.
3. Price P, Witt C, Allcock R, et al: The genetic basis for the association of the 8.1 ancestral haplotype (A1, B8, DR3) with multiple immunopathological diseases 167:257–274, 1999.
4. Lahita RG. Introduction. In: Lahita RG, ed. Systemic Lupus Erythematosus. New York: John Wiley and Sons. 1987; 1-3. (Fifth edition published 2010)
5. Benedek TG. Historical background of discoid and systemic lupus erythematosus. In: Wallace DJ, Hahn BH, eds. Dubois' Lupus Erythematosus. Philadelphia: Lippincott Williams & Wilkins / Wolters Kluwer, 7th edition, 2007, pp. 2-15. (Eighth edition published 2012)
6. Iglesias, A. Los primeros pasos (The First Steps). In: Gamarra A. Historia del Lupus y del Sindrome Antifosfolipídico (History of Lupus and of the Antiphospholipid Syndrome). Barranquilla,

Colombia. Universidad Simón Bolivar, 2011; 33-118 (Second edition published 2011)

7. Boltzer JW. Systemic lupus erythematosus. I. Historical aspects. MD State Med J 1983; 37:439.
8. Kaposi MH. Neue Beitrage zur Keantiss des lupus erythematosus. Arch Dermatol Syphilol 1872; 4:
9. Kirou KA, Lee C, George S, et al: Activation of the interferon-alpha pathway identifies a subgroup of systemic lupus erythematosus patients with distinct serologic features and active disease 52(5):1491–1503, 2005.
10. Bennett L, Palucka AK, Arce E, et al: Interferon and granulopoiesissignatures in systemic lupus erythematosus blood ,197(6):711–723, 2003.
11. Baechler EC, Batliwalla FM, Karypis G, et al: Interferon-inducible gene expression signature in peripheral blood cells of patients with severe lupus , 2610–2615, 2003.
12. Crow MK, Kirou KA, Wohlgemuth J: Microarray analysis of interferon-regulated genes in SLE,:481–490,2003.
13. Gorelik G, Fang JY, Wu A, et al: Impaired T cell protein kinase Cdelta activation decreases ERK pathway signaling in idiopathic and hydralazine-induced lupus, 179(8):5553–5563, 2007.

14. Moon UY, Park SJ, Oh ST, et al: Patients with systemic lupus erythematosus have abnormally elevated Epstein-Barr virus load in blood, 6(4):R295–302, 2004.
15. Poole BD, Templeton AK, Guthridge JM, et al: Aberrant Epstein-Barr viral infection in systemic lupus erythematosus, 337–342, 2009.
16. Peters AL, Stunz LL, Meyerholz DK, et al: Latent membrane protein 1, the EBV-encoded oncogenic mimic of CD40, accelerates autoimmunity in B6.Sle1 mice, 4053–4062, 2010.
17. Kang I, Quan T, Nolasco H, et al: Defective control of latent Epstein-Barr virus infection in systemic lupus erythematosus, 1287–1294, 2004.
18. Costenbader KH, Kim DJ, Peerzada J, et al: Cigarette smoking and the risk of systemic lupus erythematosus: a meta-analysis, 849–857, 2004.
19. Gilliam JN, Sontheimer RD: Distinctive cutaneous subsets in the spectrum of lupus erythematosus, 4:471–475,1981.
20. Sontheimer RD: The lexicon of cutaneous lupus erythematosus: a review and personal perspective on the nomenclature and classification of the cutaneous manifestations of lupus erythematosus 6:84–95, 1997.

21. Gilliam JN, Sontheimer RD: Skin manifestations of SLE, 8:207–218, 1982.
22. Chaudhry SI, Murphy LA, White IR: Subacute cutaneous lupus erythematosus a paraneoplastic dermatosis 655–658, 2005.
23. Perniciaro C, Randle HW, Perry HO: Hypertrophic discoid lupus erythematosus resembling squamous cell carcinoma, 21:255–257, 1995.
24. Vassileva S: Bullous systemic lupus erythematosus, 22:129–138, 2004.
25. Grossman JM: Lupus arthritis, 23:495–506, 2009.
26. Tsokos GC, Moutsopoulos HM, Steinberg AD: Muscle involvement in systemic lupus erythematosus, 766–768, 1981.
27. Fialho SC, Bonfa E, Vitule LF, et al: Disease activity as a major risk factor for osteonecrosis in early systemic lupus erythematosus, 239–244, 2007.
28. Danila MI, Pons-Estel GJ, Zhang J, et al: Renal damage is the most important predictor of mortality within the damage index: data from LUMINA LXIV, a multiethnic US cohort, 542–545, 2009.
29. Weening JJ, D'Agati VD, Schwartz MM, et al: The classification of glomerulonephritis in systemic lupus erythematosus revisited, 241–250, 2004.

30. Good JT Jr, King TE, Antony VB, Sahn SA: Lupus pleuritis: clinical features and pleural fluid characteristics with special reference to pleural fluid antinuclear antibodies, 714–718, 1983.
31. Matthay RA, Schwarz MI, Petty TL, et al: Pulmonary manifestations of systemic lupus erythematosus: review of twelve cases of acute lupus pneumonitis, 397–409, 1975.
32. Hoffbrand BI, Beck ER: Unexplained dyspnea and shrinking lungs in systemic lupus erythematosus, 1273–1277, 1965.
33. Crozier IG, Li E, Milne MJ, Nicholls MG: Cardiac involvement in systemic lupus erythematosus detected by echocardiography, 1145–1148, 1990.
34. Sultan SM, Ioannou Y, Isenberg DA: A review of gastrointestinal manifestations of systemic lupus erythematosus, 917–932, 1999.
35. Nesher G, Breuer GS, Temprano K, et al: Lupus-associated pancreatitis, 260–267, 2006.
36. Füreder W, Firbas U, Nichol JL, et al: Serum thrombopoietin levels and anti-thrombopoietin antibodies in systemic lupus erytheatosus,221–226, 2002.
37. Krishnan E: Stroke subtypes among young patients with systemic lupus erythematosus, 118:1415.e1–e7, 2005;Davies JB, Rao PK: Ocular manifestations of systemic lupus erythematosus,512–518, 2008.

38. Ferreira S, D’Cruz DP, Hughes GR: Multiple sclerosis, neuropsychiatric lupus and antiphospholipid syndrome: 434–439, 2005.
39. Kratzsch J, Pulzer F. Thyroid gland development and defects. 2008;22:57-75.
40. Bizhanova A, Kopp P. Minireview: the sodium-iodide symporter NIS and pendrin in iodide homeostasis of the thyroid. 2009;150:1084-1090.
41. Taurog A, Dorris ML, Doerge DR. Mechanism of simultaneous iodination and coupling catalyzed by thyroid peroxidase. 1996; 330:24-32.
42. Mandel SJ, Brent GA, Larsen PR. Levothyroxine therapy in patients with thyroid disease. 1993;119:492-502.
43. Carr K, Mcleod DT, Parry G, et al. Fine adjustment of thyroxine replacement dosage: comparison of the thyrotrophin releasing hormone tests using a sensitive thyrotrophin assay with measurement
44. Fliers E, Wiersinga WM. Myxedema coma..2003;4:137-141.
45. Imaizumi M, Akahoshi M, Ichimaru S, et al. Risk for ischemic heart disease and all-cause mortality in subclinical hypothyroidism. 2004; 89:3365-3370.

46. Kakehasi AM ,Dias.VN ,Duaret JE , Lanna CC , de Calvathom; Thyroid abnormalities in systemic Lupus Erythematosus 2006 : 64(6);375-9
47. Zakari Z , Sandooghi M .Thyroid disorders in systemic Lupus Erythematosus patients in Southeast Iran . Shiraz E -2010 ;11:1
48. Shahin A , Moustafa H , Mahmouds,Thyroid hormones and thyroid stimulating hormones in Egyptian patients with systemic Lpus Erythematosus correlation between secondary hypothyroidism and Neuropsychiatric systemic Lpus Erythematosus , 2002:12:338-41

ANNEXURES

"ASSESSMENT OF THYROID FUNCTION IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS AND ITS CLINICAL CORRELATION "

PROFORMA

NAME: **AGE/SEX :**

ADDRESS : **OCCUPATION :**

PRESENTING COMPLAINTS :

- Fever
- Joint pain
- Easy fatiguability
- Breathlessness / Orthopnea
- Paroxysmal nocturnal dyspnea
- Abdominal pain / abdominal distension
- Heat intolerance
- Cold intolerance
- Weight gain
- Weight loss
- Nervousness
- Palpitation
- Tremor
- Seizure
- Altered sensorium
- Constipation
- Menstrual disturbances
- Skin rash

- Oral ulcer
- Photosensitivity
- Drug intake

PAST HISTORY:

- Heart disease
- Hypertension
- Diabetes
- Pulmonary tuberculosis
- Bronchial asthma
- Epilepsy

GENERAL EXAMINATION :

- Built
- Nourishment
- pallor
- Icterus
- Cyanosis
- Clubbing
- Lymphadenopathy
- Pedal edema
- Oral cavity
- Skin manifestations
- Thyroid

VITAL SIGNS :

PR-

BP-

RR-

SYSTEMIC EXAMINATIONS :

CARDIOVASCULAR SYSTEM :

RESPIRATORY SYSTEM:

PER ABDOMEN:

CENTRAL NERVOUS SYSTEM:

INVESTIGATIONS :

- Haemogram
- ESR
- Renal function test
- Liver function test
- Urine routine
- Lipid profile
- Electrocardiogram
- Chest X-ray
- Anti nuclear antibody
- Anti ds -DNA
- FreeT3 and Free T4
- TSH
- USG Neck

ABBREVATIONS

ACE	-	Angiotensin Converting Enzyme
ANA	-	Anti nuclear Antibody
Anti ds DNA	-	Anti double stranded DNA
Anti-Sm	-	Anti Smith
APC	-	Antigen Presenting Cells
CoA	-	Coactivators
CoR	-	Co -Receptor protein
DIT	-	Diiodotyrosine
ECG	-	Electrocardiogram
GIT	-	Gastrointestinal Tract
FT3	-	Free Triiodothyronine
FT4	-	Free thyroxine
HLA	-	Human Leukocyte Antigen
IIF	-	Indirect Immunofluorescence
LFT	-	Liver function test
MHC	-	Major Histocompatibility Complex
MIT	-	Monoiodotyrosine
NO	-	Nitric oxide
PE	-	Pleural effusion
RA	-	Rheumatoid Arthritis

RFT	-	Renal function test
ROS	-	Reactive oxygen species
RT3	-	Reverse Triiodothyronine
RXR	-	Retinoid X Receptor
SLE	-	Systemic Lupus Erythematosus
TBG	-	Thyroxine Binding Globulin
TG	-	Thyroglobulin
TPO	-	Thyroid Peroxidase
TRE	-	Thyroid hormone Response Elements
TRH	-	Thyrotropin - Releasing Hormone
TR	-	Thyroid hormone Receptor
TSH	-	Thyroid Stimulating Hormone

INFORMATION SHEET

TITLE :

"ASSESSMENT OF THYROID FUNCTION IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS AND ITS CLINICAL CORRELATION"

Name of Investigator : Name of Participant :

Purpose of Research : Assessment of thyroid function in patients with SLE and its clinical correlation .

S**tudy Design :**Prospective Observational Study

Study Procedures : Patient will be subjected to routine investigations, Chest X ray, ANA , Anti ds -DNA& USG neck & free T3, freeT4, TSH and outcomes analysed

Possible Risks : No risks to the patient

Possible benefits

To patient : Patient is provided a means of assessing the pathology their disease and also as a means of early identification.

To doctor & to other people : If this study gives positive results, it can help to emphasize the role of routine thyroid function testing in patients with SLE. This will help in providing better and early diagnosis to other patients in future.

Confidentiality of the information obtained from you : The privacy of the patients in the research will be maintained throughout the study. In the event of any publication or presentation resulting from the research, no personally identifiable information will be shared

Can you decide to stop participating in the study : Taking part in this study is voluntary. You are free to decide whether to participate in this study or to withdraw at any time

How will your decision to not participate in the study affect you : Your decision will not result in any loss of benefits to which you are otherwise entitled.

Signature of Investigator: Signature of the participant:

Date :

Place :

PATIENT CONSENT FORM

Study Detail : **"ASSESSMENT OF THYROID FUNCTION IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS AND ITS CLINICAL CORRELATION"**

Study Centre : Rajiv Gandhi Government General Hospital, Chennai.

Patient's Name :

Patient's Age :

In Patient Number :

Patient may check (☑) these boxes

I confirm that I have understood the purpose of procedure for the above study. I have the opportunity to ask question and all my questions and doubts have been answered to my complete satisfaction. ❑

I understand that my participation in the study is voluntary and that I am free to withdraw at any time without giving reason, without my legal rights being affected. ❑

I understand that sponsor of the clinical study, others working on the sponsor's behalf, the ethical committee and the regulatory authorities will not need my permission to look at my health records, both in respect of current study and any further research that may be conducted in relation to it, even if I withdraw from the study I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published, unless as required under the law. I agree not to restrict the use of any data or results that arise from this study. ❑

I agree to take part in the above study and to comply with the instructions given during the study and faithfully cooperate with the study team and to immediately inform the study staff if I suffer from any deterioration in my health or well being or any unexpected or unusual symptoms. ❑

I hereby consent to participate in this study ❑

I hereby give permission to undergo complete clinical examination and diagnostic tests including hematological, biochemical, radiological tests. ❑

Signature/thumb impression

Patient's Name and Address:

Signature of Investigator

Study Investigator's Name :

Dr.VELVIZHI.M

ஆராய்ச்சி தகவல் தாள்

இராஜீவ் காந்தி அரசு பொது மருத்துவமனைக்கு வரும் செஞ்சரும பல்லுறுப்பு நோயினால் பாதிக்கப்பட்ட நோயாளிகளில் குருதி சீரத்தில் தைராய்டு ஹார்மோனின் அளவினை கணக்கிடுவதின் பயன் பற்றிய ஆய்வு.

நாங்கள் உங்களிடமிருந்து பெறும் மாதிரிகள் முக்கியமானவை என்பதை தெரிவிக்கின்றோம்.

நீங்கள் இந்த ஆய்விற்கு தகுதியானவர்களாக இருக்கும் பட்சத்தில் தங்களிடமிருந்து 8 மி.லி. அளவு இரத்தம் பெற்று அதில் இரத்தப் பரிசோதனைகள் செய்யப்படும் (டி3, டி4, டி.எஸ்.எச்). கழுத்து ஸ்கேன் (அல்ட்ராசவுண்ட்), பரிசோதனைகளின் மூலம் தைராய்டு எனும் ஹார்மோன் அளவு கணக்கிடப்படும்.

தங்களுடைய தனிப்பட்ட தகவல்களோ அல்லது தங்களின் உடல்நிலை பற்றிய குறிப்புகளோ எவ்வித வெளியீடாகவோ அல்லது அறிக்கையாகவோ வெளியிடப்படமாட்டாது என்பதை தெரிவித்துக் கொள்கிறோம்.

இந்த ஆராய்ச்சியில் பங்கேற்பது தங்களுடைய விருப்பத்தின் பேரில் தான் இருக்கிறது. மேலும் நீங்கள் எந்நேரமும் இந்த ஆராய்ச்சியிலிருந்து பின்வாங்கலாம் என்பதையும் தெரிவித்துக்கொள்ளலாம்.

இந்த சிறப்புப் பரிசோதனைகளின் முடிவுகளை ஆராய்ச்சியின் போது அல்லது ஆராய்ச்சியின் முடிவின் போது தங்களுக்கு அறிவிப்போம் என்பதையும் தெரிவித்துக்கொள்கிறோம்.

ஆராய்ச்சியாளர் கையொப்பம் பங்கேற்பாளர் கையொப்பம்

தேதி:

INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE, CHENNAI-3

EC Reg No.ECR/270/Inst./TN/2013
Telephone No. 044 25305301
Fax : 044 25363970

CERTIFICATE OF APPROVAL

To
Dr.M.Velvizhi
Post Graduate M.D.(General Medicine)
Madras Medical College
Chennai 600 003

Dear Dr.M.Velvizhi,

The Institutional Ethics Committee has considered your request and approved your study titled **"Assessment of thyroid function in patients with systemic lupus erythematosus and its clinical correlation" No.23062015.**

The following members of Ethics Committee were present in the meeting held on 09.06.2015 conducted at Madras Medical College, Chennai-3.

1. Prof.C.Rajendran, M.D.,	: Chairperson
2. Prof.R.Vimala, M.D., Dean, MMC, Ch-3	: Deputy Chairperson
3. Prof.B.Kalaiselvi, M.D., Vice-Principal, MMC, Ch-3	: Member Secretary
4. Prof.B.Vasanthi, M.D., Prof. of Pharmacology, MMC	: Member
5. Prof.P.Raghumani, M.S., Professor of Surgery, MMC	: Member
6. Prof.Md.Ali, M.D., DM., Prof. & HOD of MGE, MMC	: Member
7. Prof.Baby Vasumathi, Director, Inst.of O&G, Ch-8	: Member
8. Prof.Ramadevi, Director, Inst.of Bio-chemistry, MMC	: Member
9. Prof.Saraswathy, M.D., Director, Pathology, MMC, Ch-3	: Member
10. Prof.K.Srinivasagalu, M.D.,Director, I.I.M. MMC, Ch-3	: Member
11. Thiru S.Rameshkumar, B.Com., MBA	: Lay Person
12. Thiru S.Govindasamy, B.A., B.L.,	: Lawyer
13. Tmt.Arnold Saulina, M.A., MSW.,	: Social Scientist

We approve the proposal to be conducted in its presented form.

The Institutional Ethics Committee expects to be informed about the progress of the study and SAE occurring in the course of the study, any changes in the protocol and patients information/informed consent and asks to be provided a copy of the final report.

Member Secretary, Ethics Committee

MEMBER SECRETARY
INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE
CHENNAI-600 003

MASTER CHART

S.NO	AGE	SEX	I.P.NO	DURATION OF DISEASE (YEARS)	WEIGHT GAIN	WEIGHT LOSS	HEAT INTOLERANCE	COLD INTOLERANCE	PALPITATION	TREMOR	SKIN CHANGES	MENSTRUAL DISTURBANCES	GIT	PSYCHIATRIC MANIFESTATION	DYSLIPIDEMIA	HEAMOGLOBIN(GM)	ECG	CHESTXRAY	ANA	ANTI ds DNA	FT3	FT4	TSH	USG NECK
1	23	F	95727	2	-	-	-	-	-	-	-	-	-	-	-	9	N	N	+	+	0.4	1.3	8.4	N
2	23	F	94123	1	-	-	-	-	-	-	-	-	-	-	-	9.4	N	N	+	+	0.3	1.4	7.6	N
3	37	F	96493	5	-	-	-	-	-	-	-	-	-	-	-	8.1	N	N	+	+	0.2	1	9.3	N
4	27	F	96963	2	-	-	-	+	-	-	-	-	-	-	-	7.5	N	N	+	+	0.4	1.3	4.1	N
5	24	F	92275	NEW	-	+	-	-	-	-	-	-	-	-	-	10.2	N	N	+	+	0.7	0.9	2.5	N
6	19	F	94551	NEW	-	+	-	-	-	-	-	-	-	-	-	9.6	N	N	+	+	0.5	1.5	3.1	N
7	15	F	60439	1	-	-	-	-	-	-	-	-	-	-	-	8.9	N	N	+	+	0.3	1.1	4	CYST
8	16	F	87403	1	-	-	-	-	-	-	-	-	-	-	-	6.2	N	N	+	+	0.6	1.7	3.5	N
9	37	F	97051	6	+	-	-	-	-	-	-	-	C	+	+	7.9	N	PE	+	+	0.01	0.2	16.4	N
10	48	F	43886	5	+	-	-	-	+	-	-	-	-	-	-	8	N	N	+	+	0.3	0.9	1.8	N
11	21	F	59681	3	-	+	-	-	-	-	-	-	-	-	-	8.4	N	N	+	+	0.5	1.2	2.6	N
12	29	F	57107	4	-	-	-	-	-	-	-	-	-	-	-	7.9	N	N	+	+	0.2	1.5	8.7	N
13	17	F	65390	1	-	-	-	-	+	-	-	-	-	-	-	5.7	N	N	+	+	0.6	1.8	2.9	N
14	20	F	80727	2	-	+	-	-	+	-	-	-	-	-	-	9.7	N	N	+	+	0.4	1.4	3.6	N
15	26	F	81507	NEW	-	+	-	-	-	-	-	-	-	-	-	10	N	N	+	+	0.5	1.1	4	N
16	22	F	80224	NEW	-	-	-	-	-	-	-	-	-	-	-	10.5	N	N	+	+	0.7	0.9	3.1	N
17	30	F	81229	4	+	-	-	+	-	-	-	-	-	-	-	8.6	N	N	+	+	0.2	1.2	1.8	N
18	26	F	79861	3	-	-	-	-	-	-	-	-	-	-	-	9.2	N	N	+	+	0.4	1.1	8.3	N
19	34	F	76549	5	-	+	-	-	+	+	-	-	-	-	-	8.1	N	N	+	+	0.5	1.6	3.2	N
20	32	F	79012	NEW	-	+	-	-	-	-	-	+	-	-	-	10.5	N	N	+	+	0.3	1.4	3.5	N
21	21	F	77834	2	-	+	-	-	-	-	-	-	-	+	-	11	N	N	+	+	0.4	1.6	2.1	N
22	19	F	71290	1	-	-	-	-	-	-	-	-	-	-	-	9.7	N	N	+	+	0.5	1.3	4.2	N
23	28	F	87652	4	+	-	-	+	-	-	-	+	C	-	-	6.2	N	N	+	+	0.02	0.1	17.6	N
24	23	F	65437	3	-	-	-	-	-	-	+	-	-	-	-	9.1	N	N	+	+	0.7	1	4.3	N
25	36	F	72983	7	-	-	-	-	-	-	-	-	-	-	-	9	N	N	+	+	0.3	1.2	9.3	N
26	40	F	66782	6	+	-	-	-	-	-	-	-	-	-	-	10.2	N	N	+	+	0.5	1.7	3.7	N
27	17	F	69354	1	-	-	-	-	-	-	-	-	-	-	-	9.6	N	N	+	+	0.8	1.2	2.9	N
28	24	F	71098	4	-	+	-	-	-	-	-	+	-	-	-	8.7	N	N	+	+	0.2	0.9	2.4	N

29	29	F	70145	3	+	-	-	-	+	-	-	-	-	-	+	7.4	N	PE	+	+	0.03	1.1	21.6	N
30	38	F	71652	5	+	-	-	-	-	-	-	-	-	+	+	10	N	N	+	+	0.6	1.4	2.1	N
31	19	F	68340	2	-	-	-	-	-	-	-	-	-	-	-	9.8	N	N	+	+	0.2	1	3.7	N
32	27	F	67891	1	-	-	-	-	-	-	-	-	-	-	-	11.2	N	N	+	+	0.4	1.5	3.1	N
33	36	F	57198	2	-	-	-	+	-	-	-	-	-	+	-	7.5	N	N	+	+	0.01	0.3	18.3	N
34	31	F	60917	4	+	-	-	-	-	-	-	-	-	-	-	8.4	N	N	+	+	0.3	1.8	4	N
35	26	F	71453	8	+	-	-	-	-	-	-	+	-	-	+	9	N	N	+	+	0.5	1	3.2	N
36	42	F	79821	5	-	-	-	-	-	-	-	-	-	-	-	8.1	N	N	+	+	0.4	1.5	8.1	N
37	30	F	64097	3	-	-	-	-	-	-	-	-	-	-	-	10.3	N	N	+	+	0.6	1.6	4	N
38	24	F	78431	3	-	-	-	+	-	-	-	-	-	-	-	11	N	N	+	+	0.2	1.8	3.2	N
39	22	F	65210	1	-	-	-	+	-	-	-	-	-	-	-	10.7	N	N	+	+	0.7	1.1	2.5	N
40	27	F	56983	3	-	-	-	-	-	-	-	-	-	-	+	7.1	N	N	+	+	0.2	1.4	9.4	N
41	35	F	59820	2	-	+	-	-	-	-	+	-	-	-	-	10.4	N	N	+	+	0.5	1.9	4.3	N
42	34	F	57531	NEW	-	-	-	-	-	-	-	-	-	-	-	9.8	N	N	+	+	0.3	1.2	3.5	N
43	31	F	70369	4	+	-	-	-	-	-	-	-	-	-	-	8.7	N	N	+	+	0.7	1.7	2.8	N
44	18	F	67891	1	-	-	-	-	-	-	-	-	-	-	-	9.5	N	N	+	+	0.4	1.5	1.8	N
45	16	F	58341	2	-	-	-	-	-	-	-	-	-	-	-	10.9	N	N	+	+	0.2	1	3.9	N
46	43	F	60118	6	+	-	-	-	-	-	-	+	-	-	-	8.2	N	N	+	+	0.6	0.9	4.3	N
47	37	F	62871	5	+	-	-	-	+	-	-	-	-	+	-	7.6	N	N	+	+	0.5	1.6	4	N
48	34	F	66439	2	-	-	-	-	-	-	-	-	C	-	-	10.2	N	N	+	+	0.4	1.8	2.6	N
49	25	F	73209	3	-	-	-	-	-	-	-	-	D	-	-	9.1	N	N	+	+	0.3	1.1	3.1	N
50	28	F	42801	4	-	-	-	-	-	-	-	-	-	-	-	6.8	N	N	+	+	0.3	1.2	7.9	N
51	20	F	65320	1	-	-	-	+	-	-	-	-	-	-	-	11.6	N	N	+	+	0.2	0.9	3.9	N
52	33	F	58720	6	-	-	-	-	-	-	-	-	-	-	+	9.5	N	N	+	+	0.4	1.6	2.1	N
53	30	F	59014	4	-	-	-	-	-	-	+	-	-	-	-	8.9	N	N	+	+	0.02	0.3	15.6	N
54	29	F	51987	NEW	-	-	-	+	-	-	-	-	-	-	-	11.2	N	N	+	+	0.5	1.4	4	N
55	34	F	73982	4	-	-	-	+	-	-	-	-	-	-	-	9.8	N	N	+	+	0.1	1.1	3.4	N
56	40	F	49824	7	+	-	-	-	-	-	-	-	-	+	-	11	N	N	+	+	0.3	1.8	2.9	N
57	36	F	69320	5	+	-	-	-	-	-	-	-	-	-	-	7.6	N	N	+	+	0.6	0.9	3.1	N
58	32	F	79381	2	-	+	-	-	-	-	-	-	-	-	-	9	N	N	+	+	0.7	1.1	2.6	N
59	29	F	71024	1	-	-	-	-	-	-	-	-	-	-	-	10.8	N	N	+	+	0.4	1.2	1.8	N
60	27	F	64689	3	-	-	-	-	+	-	-	+	D	-	-	11	N	N	+	+	0.3	1.7	4.3	N
61	31	F	69317	4	-	-	-	-	-	-	-	-	-	-	-	9.2	N	N	+	+	0.2	1.3	8.6	N
62	21	F	53901	NEW	-	-	-	-	-	-	-	-	-	-	-	10.6	N	N	+	+	0.4	1.5	4.2	N
63	28	F	50487	3	-	-	-	-	-	-	-	-	-	-	+	9.9	N	N	+	+	0.2	1.6	9.1	N
64	36	F	42903	4	-	-	-	-	-	-	-	-	-	-	-	10.1	N	N	+	+	0.3	1.2	8.9	N
65	41	F	43691	1	-	-	-	-	-	-	-		-	-	-	11.6	N	N	+	+	0.6	1.9	3.7	N
66	43	F	46182	5	+	-	-	-	-	-	-	+	C	-	-	9.8	N	N	+	+	0.2	1.7	2.8	N
67	25	F	49710	3	-	-	-	-	-	-	-	-	-	-	-	8.5	N	N	+	+	0.5	0.9	3.5	N
68	22	F	40153	NEW	-	-	+	+	-	-	-	+	-	-	-	10.6	N	N	+	+	0.1	1.3	2.1	N
69	20	F	58670	2	-	-	+	+	-	-	-	-	-	-	-	9.1	N	N	+	+	0.4	1.8	4.3	N

70	19	F	53804	3	-	-	-	-	-	-	-	-	-	-	-	11.4	N	N	+	+	0.8	1.5	3	N
71	39	F	40183	6	-	-	-	-	-	-	-	-	-	-	+	8.3	N	N	+	+	0.3	1	1.9	N
72	33	F	39568	4	-	-	-	-	-	-	-	-	-	-	+	9	N	N	+	+	0.4	0.9	9.4	N
73	26	F	33982	NEW	-	-	-	-	-	-	-	-	-	-	-	10.6	N	N	+	+	0.2	1.4	4.7	
74	18	F	60173	NEW	-	-	-	-	-	-	-	+	-	-	-	9.5	N	N	+	+	0.5	1.2	4	N
75	25	F	50914	1	-	-	-	-	-	-	-	-	-	-	-	11.6	N	N	+	+	0.7	1.7	3.4	N
76	24	F	79801	4	+	-	-	-	-	-	-	-	-	-	-	10	N	N	+	+	0.1	1.2	4.1	N
77	22	F	40913	2	-	-	-	-	-	-	-	-	-	-	-	9.7	N	N	+	+	0.4	0.9	3.6	N
78	20	F	44071	NEW	-	-	-	-	-	-	-	-	-	-	-	12	N	N	+	+	0.2	1	1.9	N
79	19	F	38619	4	-	+	-	-	-	-	-	-	-	-	-	7.9	N	N	+	+	0.5	1.3	4..0	N
80	29	F	32901	3	-	-	-	+	-	-	+	-	-	-	+	8.2	N	PE	+	+	0.02	0.1	26.4	N
81	33	F	49281	2	-	-	-	-	-	-	-	-	-	-	-	11	N	N	+	+	0.3	1.8	4.2	N
82	30	F	45938	2	-	-	-	-	-	-	-	+	-	-	-	10.1	N	N	+	+	0.1	1.5	3.6	N
83	27	F	75130	5	+	-	-	-	-	-	-	-	-	+	-	8	N	N	+	+	0.4	1.8	3.9	N
84	21	F	70912	NEW	-	-	-	-	-	-	-	-	-	-	-	7.1	N	N	+	+	0.3	1.1	2.8	N
85	29	F	52016	3	-	-	-	-	-	-	-	-	-	-	-	8.2	N	N	+	+	0.1	1.6	7.2	N
86	35	F	59203	NEW	-	-	-	-	-	-	-	-	-	-	-	11.6	N	N	+	+	0.4	1.3	4	N
87	37	F	56715	4	-	-	-	-	-	-	-	-	-	-	-	8.1	N	N	+	+	0.6	1.7	4.1	N
88	26	F	51082	3	+	-	-	-	-	-	-	-	-	-	+	7	N	N	+	+	0.01	0.2	21.4	N
89	18	F	49310	1	-	-	-	-	-	-	-	-	-	-	-	6.9	N	N	+	+	0.4	1	2.9	N
90	34	F	48731	2	-	-	-	+	-	-	-	-	-	-	-	10.7	N	N	+	+	0.5	1.5	3.6	N
91	41	F	30017	6	-	-	-	-	+	-	+	-	-	-	-	9	N	N	+	+	0.2	1.9	4.2	N
92	34	F	39163	5	-	-	-	-	-	-	-	-	-	-	+	9.5	N	N	+	+	0.4	0.9	9.6	N
93	23	F	37610	3	-	-	-	-	-	-	-	-	-	-	-	8.6	N	N	+	+	0.5	1.2	3.9	N
94	36	F	30926	4	+	-	-	-	-	+	-	-	-	-	-	7.9	N	N	+	+	0.2	1.5	4.1	N
95	31	F	87431	2	-	+	-	-	-	-	-	+	-	-	-	11	N	N	+	+	0.3	1.3	4.2	N
96	30	F	80327	1	-	-	-	-	-	-	-	-	-	-	-	12	N	N	+	+	0.4	1.2	3.7	N
97	26	F	71205	3	-	-	-	-	-	-	-	-	-	-	-	9.7	N	N	+	+	0.2	1	8.5	N
98	29	F	76204	1	-	-	-	-	-	-	-	-	-	-	-	8.9	N	N	+	+	0.5	1.4	4	N
99	38	F	56292	4	+	-	-	-	-	+	-	-	-	-	-	10.2	N	N	+	+	0.4	1.6	3.8	N
100	17	F	43209	NEW	-	-	-	-	-	-	-	-	-	-	-	11.4	N	N	+	+	0.5	1.2	2.7	N

C- CONSTIPATION , D- DIARRHOEA, PE - PLEURAL EFFUSION, N - NORMAL

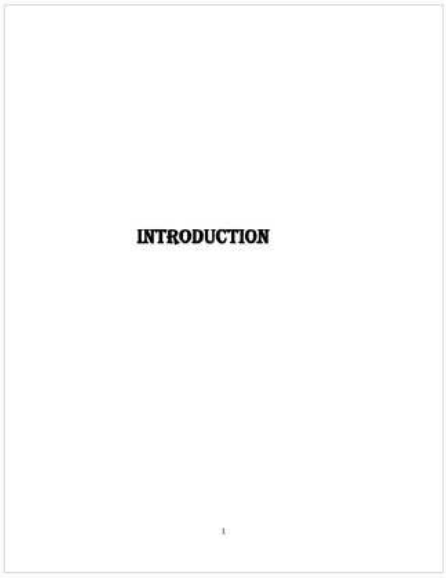
turnitin

Digital Receipt

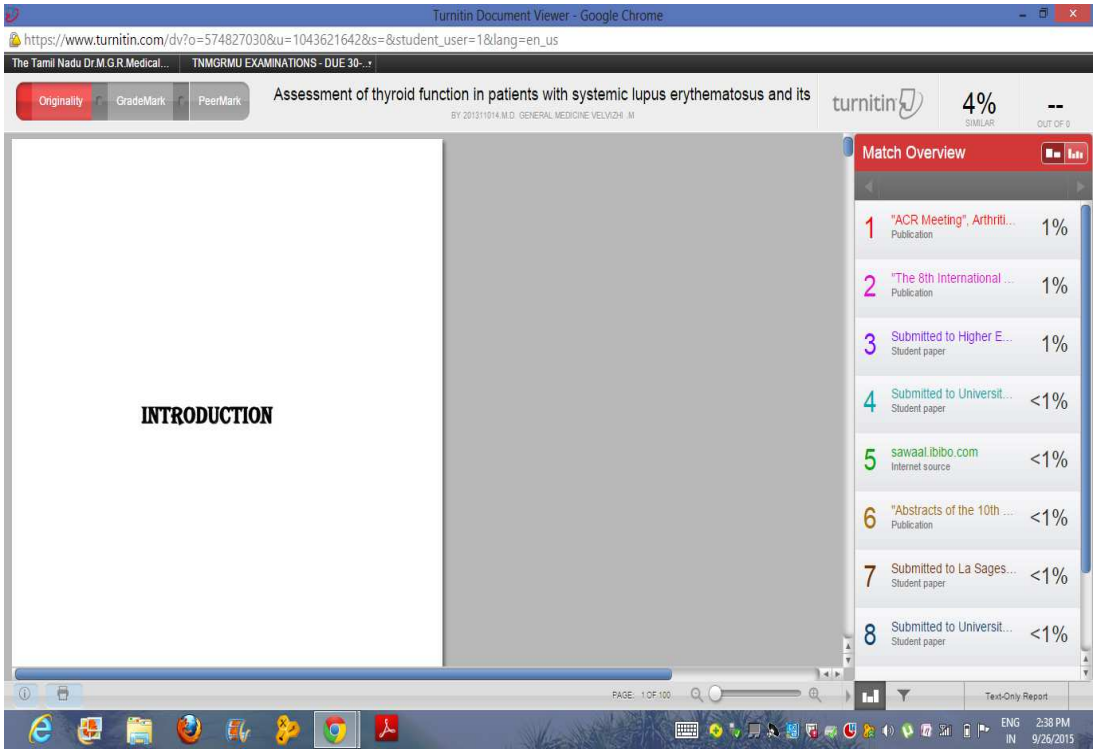
This receipt acknowledges that Turnitin received your paper. Below you will find the receipt information regarding your submission.

The first page of your submissions is displayed below.

Submission author:	201311014.m.d. General Medicine V..
Assignment title:	TNMGRMU EXAMINATIONS
Submission title:	Assessment of thyroid function in ...
File name:	review_liter.docx
File size:	10.62M
Page count:	100
Word count:	5,282
Character count:	31,107
Submission date:	25-Sep-2015 02:18PM
Submission ID:	574827030



INTRODUCTION


Turnitin Document Viewer - Google Chrome
https://www.turnitin.com/dv?o=574827030&u=1043621642&s=&student_user=1&lang=en_us
The Tamil Nadu Dr.M.G.R.Medical...
TNMGRMU EXAMINATIONS - DUE 30-...
Originality
GradeMark
PeerMark
Assessment of thyroid function in patients with systemic lupus erythematosus and its
BY 201311014.M.D. GENERAL MEDICINE VELVIZHI .M
turnitin
4%
SIMILAR
--
OUT OF 0
INTRODUCTION
Match Overview
1 "ACR Meeting", Arthriti... Publication 1%
2 "The 8th International ... Publication 1%
3 Submitted to Higher E... Student paper 1%
4 Submitted to Universit... Student paper <1%
5 sawaal.ibibo.com Internet source <1%
6 "Abstracts of the 10th ... Publication <1%
7 Submitted to La Sages... Student paper <1%
8 Submitted to Universit... Student paper <1%
PAGE: 1 OF 100
Text-Only Report
ENG
IN
2:38 PM
9/26/2015